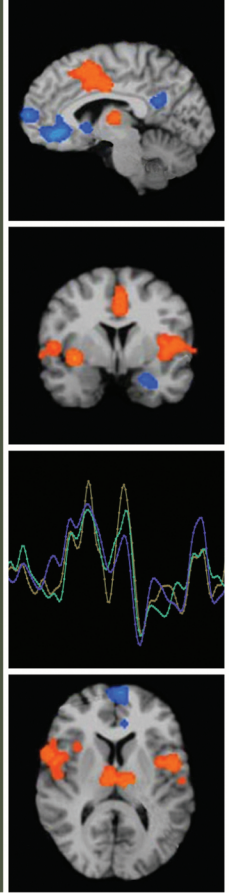


Second Edition

# Medical Acupuncture

A Western Scientific Approach



Edited by  
Jacqueline Filshie  
Adrian White  
Mike Cummings



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Foreword by  
John C Longhurst

# Medical Acupuncture

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*Senior Content Strategist:* Rita Demetriou-Swanwick

*Content Development Specialist:* Nicola Lally

*Project Manager:* Andrew Riley

*Designer/Design Direction:* Christian Bilbow

*Illustration Manager:* Emily Constantino

*Illustrator:* MPS North America

S E C O N D   E D I T I O N

# Medical Acupuncture

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## A Western Scientific Approach

Edited by

**JACQUELINE FILSHIE MBBS FRCA DipMedAC**

Consultant Anaesthetist and Honorary Senior Lecturer  
The Royal Marsden NHS Foundation Trust  
The Lister Hospital  
London, UK

**ADRIAN WHITE MA MD BM BCh**

Honorary University Fellow, Primary Care Group  
Institute of Translational and Stratified Medicine (ITSMED)  
University of Plymouth, UK  
(formerly) Editor, Acupuncture in Medicine

**MIKE CUMMINGS MB ChB DipMedAc**

Medical Director  
British Medical Acupuncture Society  
Royal London Hospital for Integrated Medicine  
London, UK

Foreword by

**JOHN C LONGHURST BS MD PhD**

ELSEVIER

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I first travelled to China in 1992 where I observed acupuncture practised by Traditional Chinese Medical (TCM) acupuncturists. Upon asking for evidence underlying this ancient technique, the practitioners firmly told me that such evidence was not necessary because acupuncture had been practised for centuries, had stood the test of time, and worked well. As an academic physician in the United States, this attitude certainly contrasted with my beliefs in the values of evidence-based medicine, a principle underlying my clinical and teaching philosophies. Two years later, upon returning to China, I was asked to consider collaborative research in acupuncture. My initial reaction was no, but my future collaborator, Dr. Peng Li, then professor and chair of the Department of Physiology at Shanghai Medical University, showed me his *curriculum vitae* containing publications in respected Western journals on the central neural mechanisms underlying acupuncture's cardiovascular actions. His interests fitted closely with my own, cardiovascular autonomic neuroscience. I subsequently invited Dr. Li to my laboratory at the University of California, Davis, where we embarked on a journey of discovery to uncover acupuncture's role in cardiovascular homeostasis.

Western medical practitioners often are sceptical of any legitimate role for acupuncture in disease treatment, including both symptom management and the underlying pathophysiology. Their concern reflects questions about TCM theory, including the absence of verification of meridians and channels, concepts like *Qi* and, in the past, the overall absence of an evidence-based approach to acupuncture treatment. Additionally, while some clinical trials show added benefit to acupuncture over and above no therapy or standard western medical approaches, often, in controlled trials, there seems to be little difference between sham (presumably reflecting placebo) and true acupuncture. Furthermore, many patients, typically a third of the population, do not respond well to acupuncture. These limitations coupled with little or no understanding of mechanisms underlying acupuncture's actions fuel debate on its role in Western medicine. Recently, however, substantial evidence has been developed supporting a role for acupuncture in clinical medicine, particularly in pain management, in combination with standard western treatments or as a stand-alone therapy. Efficacy in other clinical conditions, like hypertension, is emerging.

The first edition of *Medical Acupuncture*, published in 1998, focused on the scientific basis of acupuncture, clearly differentiating between modern western approaches and those based on TCM principles. The first edition highlighted the need for stronger clinical evidence since so much of the clinical literature was not rigorous.

The second edition of *Medical Acupuncture* builds on the first. First and foremost, all chapters are updated and expanded. For example, the number of chapters devoted to clinical medicine have expanded threefold from seven to twenty-one. This represents not just the explosion of research but also the recognition of the many areas of potentially useful acupuncture application, in addition to pain for which there has been long-standing support. New methods of study like neuroimaging and the critical role of acupuncture's central and peripheral neural and local tissue actions provide perspectives on new needling approaches and reflect our modern understanding of acupuncture's mechanisms of actions. Expansion of clinical information encompassing a wide range of disciplines ranging from dentistry to veterinary medicine highlights our new knowledge of acupuncture's role in many areas of clinical medicine. Importantly, this new edition includes critical discussion of not just acupuncture's clinical usefulness alongside standard Western approaches but also limitations of our understanding both in terms of the absence of current information and its inaction in certain patients. Commentary and analysis in the second edition, in my view, is often greater than that present for many so-called standard Western approaches.

I predict that this book will have a major impact on the field of western medicine. Perhaps, the impact of this text will be greatest on the new generation of physicians, who often appear to be most open to nonstandard approaches to treatment. I am not as sure about *Medical Acupuncture's* future influence on acupuncturists trained in and practising TCM theory. These individuals, who regularly incorporate tongue and pulse diagnosis, in my experience are much less open to modern standardised scientific approaches. However, I am sure that the evidence contained in this second edition will at the very least raise the consciousness of all who read it about the broad understanding we now have of acupuncture and its known and emerging roles in medical therapy.

***John C. Longhurst, BS MD PhD***

Professor of Medicine, Physiology and  
Biophysics and Pharmacology  
(Formerly) Director of Samueli Center  
Samueli Center for Integrative Medicine  
University of California, Irvine, USA

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We especially wish to acknowledge the sincere friendship of John Thompson (who died while this edition was being prepared) over many years, and his outstanding contributions to the acupuncture community. John's clear thinking, his erudite teaching and his research on the clinical use and mechanisms of both acupuncture and transcutaneous electrical nerve stimulation have enlightened generations of students of Western medical acupuncture, and helped make it an increasingly acceptable part of conventional medicine.

The Editors are deeply grateful to each of the authors of chapters in the second edition of this book, who have contributed to this work so generously with their time, their effort and their expertise. We know there are many others throughout the world who have helped steer acupuncture towards a scientific understanding, but who are not represented in this book, and we acknowledge their contribution to the overall project.

We also recognise the role of the British Medical Acupuncture Society and its many officers and members in continuing this process of scientific evaluation of an ancient technique. Some of our Society colleagues are represented as authors here and others (too many to mention) have made other significant contributions to the Western medical acupuncture movement.

We are grateful to the staff of Elsevier for making this new edition possible and, most particularly, to Nicola Lally and Andrew Riley, whose support and attention to detail have been outstanding.

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## **Eric F Anders MD**

Department of Pediatrics, Carl Gustav Carus  
University Hospital, Dresden, Germany

## **G David Baxter BSc DPhil MBA MCSP**

Professor and Dean, Centre for Health,  
Activity and Rehabilitation Research,  
School of Physiotherapy, University of  
Otago, Dunedin, New Zealand

## **Anthony Campbell MRCP DipMedAc**

Retired Consultant Physician, Royal London  
Hospital for Integrated Medicine,  
London, UK

## **Clare Donnellan MSc MCSP Dip Shiatsu**

Specialist Neuro-Physiotherapist, Nottingham  
University Hospitals NHS Trust,  
Nottingham, UK

## **Paul Farquhar-Smith MA MB BChir FRCA PhD FFPMRCA FFICM**

Consultant in Anaesthesia and Pain Medicine,  
The Royal Marsden NHS Foundation  
Trust, London, UK

## **Leanne Field BAH BScN RN**

Public Health Nurse, Middlesex London  
Health Unit, London, ON, Canada;  
(formerly) Medical Acupuncture Program  
Coordinator, Hamilton, ON, Canada

## **Jens Foell MD MRCPG DFFP DipMedAc**

Senior Honorary Clinical Lecturer, Queen  
Mary University of London, Barts and  
The London School of Medicine and  
Dentistry, The Blizzard Institute, Centre  
for Primary Care and Public Health,  
London, UK

## **Max Forrester MB ChB MSc WMA**

Physician Acupuncturist, Taunton, UK

## **Jonathan E Freedman MBBS MRCPG DCH DRCOG DipMedAc PgCert WMA**

General Practitioner, St Albans, UK

## **David J Grant MA MBBS FRCPE**

Consultant Physician in Medicine for the  
Elderly, NHS Lothian, Edinburgh UK

## **Rajesh Gupta MBBS MD FRCA EDRA FFPMRCA**

Consultant Anaesthesia and Pain  
Management, Hillingdon Hospitals NHS  
Foundation Trust, London, UK

## **Richard E Harris PhD**

Associate Professor, Department of  
Anesthesiology, University of Michigan,  
Ann Arbor, USA

## **Gale A Harvey RGN BSc**

Nurse Acupuncturist, Nottingham, UK

## **Simon Hayhoe MSc MBBS MRCA DA FICAE**

Medical Acupuncturist, Pain Management  
Department, University Hospital,  
Colchester; Consultant Anaesthetist and  
Medical Acupuncturist, North Essex  
Partnership University NHS Trust,  
Chelmsford, UK

## **Enoch Ho PT MPT CAFCI FCMAC**

Clinical Assistant Professor, FHS, McMaster  
University, Hamilton, Canada

## **Mark I Johnson BSc PhD**

Professor of Pain and Analgesia, Faculty of  
Health and Social Sciences, Leeds Beckett  
University, Leeds, UK

## **Stefanie Joos MD PhD**

Medical Director, Institute of General  
Practice and Interprofessional Care,  
Eberhard Karls Universitaet Tuebingen,  
Tuebingen, Germany

## **Norman W Kettner DC DACBR DCBCN FICC**

Chair, Department of Radiology, Logan  
University, Chesterfield, USA

## **Graham Leng MB ChB BSc Dip Pall Med**

Consultant in Palliative Medicine,  
Hospice of the Good Shepherd,  
Chester, UK

## **Samantha Lindley BVSc MRCVS**

Associate Lecturer, Glasgow University  
Veterinary School, Glasgow, UK

**John C Longhurst BS MD PhD**

Professor of Medicine, Physiology and Biophysics and Pharmacology; (formerly) Director of Samueli Center for Integrative Medicine, University of California, Irvine, USA

**Irène Lund RPT PhD**

Lecturer, Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

**Thomas Lundeborg MD PhD**

Senior Consultant, Pain Rehabilitation, Danderyds Hospital Stockholm, Sweden; Medical advisor, Medeon, Malmö, Sweden; Editor in Chief, Acupuncture and Related Therapies, Elsevier, Malmö, Sweden

**Alexander Macdonald MBBS DLO**

Medical Practitioner, Bristol, UK

**David F Mayor MA BAc MBACc**

Visiting Research Associate (formerly Hon Research Fellow), Department of Physiotherapy, School of Health and Social Work, University of Hertfordshire, Hatfield, UK

**Suzanne M McDonough PhD HDipHealthcare (Acupuncture) BPhysio**

Professor of Health and Rehabilitation, Ulster University, UK; Advanced Member of Acupuncture Association of Physiotherapy

**Vitaly Napadow PhD LicAc**

Associate Professor, Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, USA

**Michele Orpen RGN BA MSc**

Nurse Acupuncturist, Nottingham, UK

**Florian Pfab MD PhD**

Professor, Departments of Dermatology and Allergy and Sports Medicine & Rehabilitation, Technische Universität Munich, Germany

**Mike Pullman MBBS FRCA**

Consultant Anaesthetist, Department of Anaesthesia, Royal Hallamshire Hospital, Sheffield, UK

**Hagen Rampes BSc MBChB FRCPsych**

Formerly Assistant Professor Psychiatry, Department of Psychiatry, University of Toronto, London, UK

**Edith Rom MBBS PhD DRCophth FRCSG DPMSA DipHyp DipAT MSc WMA**

Ophthalmologist & Medical Acupuncturist Wye Valley Trust, Hereford, UK

**Patricia B Ronan PhD MSc PCMedEd RMN**

Research Fellow, Complementary Medicine and Mental Health, Speldhurst, UK

**Carolyn Rubens BA MBBS MRCGP DipMedAcu**

General Practitioner and Medical Acupuncturist, Herstmonceux Integrative Health Centre, Sussex; Honorary Pain Specialist, Royal Marsden Hospital, London UK

**Suzanne J Scott BSc DC RAc**

Doctor of Chiropractic, Registered Acupuncturist, Cambridge, Canada

**Caroline A Smith PhD MSc BSc LicAc**

Professor, National Institute of Complementary Medicine, Western Sydney University, Sydney, Australia

**Elisabet Stener-Victorin PhD**

Associate Professor, Department of Physiology and Pharmacology, Reproductive Endocrinology and Metabolism, Karolinska Institutet, Stockholm, Sweden

**Konrad Streitberger MD**

Consultant Anaesthetist Head of Pain Therapy, University Department of Anaesthesiology and Pain Therapy, University Hospital of Bern, Bern, Switzerland

**M L Tom Thayer BChD LDS RCS FDS RCPS MA MedEd FHEA**

Consultant and Honorary Senior Lecturer in Oral Surgery, Liverpool University Dental Hospital, Liverpool, UK

**John W Thompson MBBS PhD FRCP<sup>†</sup>**

Emeritus Professor of Pharmacology, University of Newcastle upon Tyne, UK

---

<sup>†</sup>Deceased

**Kien Vinh Trinh MD MSc FCFP FRSS Dip Sports Med**

Clinical Professor and Chair, MD Admissions,  
McMaster University; Medical Director,  
Boxing Canada, Hamilton, Canada

**Taras I Usichenko MD PhD**

Professor, Department of Anesthesia,  
Micheal DeGroote School of Medicine,  
McMaster University, Hamilton, Canada

**Linda Vixner PhD**

Physiotherapist, and Senior Lecturer in  
Medical Science, Dalarna University  
Stockholm, Sweden

**Lyn Williamson BM BCh MA MRCGP FRCP**

Consultant Rheumatologist, Great Western  
Hospital, Swindon, UK

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# ABBREVIATIONS

<b>CI</b>	confidence interval
<b>EA</b>	electroacupuncture
<b>GP</b>	general practitioner
<b>MA</b>	manual acupuncture
<b>MRI</b>	magnetic resonance imaging
<b>NICE</b>	National Institute for Health and Care Excellence
<b>NSAID</b>	non-steroidal anti-inflammatory drug
<b>OA</b>	osteoarthritis
<b>QoL</b>	quality of life
<b>RCT</b>	randomised controlled trial
<b>SMD</b>	standardised mean difference
<b>TCA</b>	traditional Chinese acupuncture
<b>TCM</b>	traditional Chinese medicine
<b>TENS</b>	transcutaneous electrical nerve stimulation
<b>VAS</b>	visual analogue scale
<b>WMA</b>	Western medical acupuncture

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# *Introduction*

## SECTION OUTLINE

- 1 Introduction 2
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# Introduction

A. White ■ M. Cummings ■ J. Filshie

## CHAPTER OUTLINE

<b>WMA: principles</b> 2	Problems in acupuncture research 7
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Acupuncture is increasingly accepted throughout the world for its valuable contribution to health care, and there is growing evidence of its lasting clinical benefit to patients, as well as its safety and cost-effectiveness. The approach known as Western medical acupuncture (WMA) is increasingly recognised and accepted within conventional medicine. Our intention in putting together a new edition of this book is to provide a science-based compendium of acupuncture mechanisms, techniques, clinical practice and evidence using the Western medical approach. This book is intended to expand on the information given in *An Introduction to Medical Acupuncture* and serve as its more advanced companion.

## WMA: principles

WMA is an approach to acupuncture based on conventional medical science, and defined as follows (White et al., 2009).

### Clinical points

#### Western medical acupuncture definition

A therapeutic modality involving the insertion of fine filiform needles; it is an adaptation of Chinese acupuncture using current knowledge of anatomy, physiology and pathology and the principles of evidence-based medicine.

The words ‘Western medical’ are included to contrast it with acupuncture used as part of Chinese medicine (traditional Chinese acupuncture, TCA), and in no way implies that this approach to acupuncture is limited to the West. Acupuncture is indebted to the Chinese for the remarkable discovery that inserting needles into the body and manipulating them can have therapeutic effects. The Chinese understood acupuncture according to the prevailing understanding of the body’s workings (microcosm) and how they relate to the world (macrocosm). As knowledge and understanding of the body developed, the old ideas were not jettisoned but absorbed, whereas

the current Western scientific tradition replaces outdated concepts when new evidence arises (Chapter 2). Although the approach of acupuncturists using TCA and those using WMA are fundamentally different, their actual practice of acupuncture is remarkably similar. And, although it is somewhat surprising that the majority of acupuncturists throughout the world still use a TCA approach, the effects of acupuncture, however applied, can be understood through mechanisms that are increasingly well known. Acupuncture is becoming plausible.

Acupuncture's modes of action, particularly those relating to pain control, involve stimulation of the nervous system, the muscular system and connective tissue. These mechanisms are now understood in some detail, so it is appropriate to start this book with a comprehensive description of peripheral mechanisms (Chapter 3) followed by detailed discussion of the effects on the brain and autonomic nervous system as well as the all-important current understanding of the mechanisms of chronic pain (Chapters 4–6).

The techniques used in WMA are relatively simple and the principles of safe and effective practice are described in the section on clinical approaches (Chapters 7–13).

Treatment is usually by sessions of manual acupuncture or electroacupuncture to needles inserted into the body or the ear; sometimes needles are retained for a week or so. We make no distinction between the terms 'dry needling' and acupuncture. The text includes chapters on the related techniques of transcutaneous electrical nerve stimulation (TENS) (Chapter 15) and laser acupuncture (Chapter 16), though clinical chapters generally consider only the evidence to needle acupuncture. This text does not systematically cover acupressure nor acupuncture point injection.

Another feature of WMA is its emphasis on scepticism in place of credulousness and rationality rather than belief. Scepticism allows us to remain unconvinced by traditional theories even when the apparent effects of acupuncture cannot be easily explained. For example, there seems no mechanism for the effect of BL67 (on the small toes) when used in pregnancy for converting breech presentation to vertex. So, although the clinical trials currently support such an effect, it is wise to remain open-minded until the results are explained or mode of action discovered.

## POINTS AND POINT SPECIFICITY

The most characteristic features of traditional acupuncture are the 'points' and the 'meridians'. Traditional charts indicate over 300 small, precisely defined 'points', and classical texts suggest using particular points for particular conditions. The WMA approach is very different and clearly set out in Chapters 7–9. There is no evidence for any consistent, universal anatomical structure at these points and known physiology does not explain the meridians. The aim in WMA is to make an appropriate stimulation of the right structure. This may be at any depth from skin, subcutaneous tissue, muscle and its surrounding connective tissue down to the periosteum. Muscle is a common target. The needle has to go somewhere, and in fact many classical 'points' are convenient locations for needling muscle – either healthy muscle in general to stimulate the afferent nerves or muscle with localised trigger points. But there is no need to restrict the insertion to 'points' only, and Chapter 8 describes an approach that virtually abandons the concept of points (except as convenience for communication), and prefers to refer to treatment 'areas'.

### Clinical points

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According to the current state of scientific knowledge, traditional concepts of points and meridians are unsubstantiated.

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Another area where WMA breaks with tradition is the concept of *point specificity* – the idea that particular points or point combinations have unique, targeted effects on remote functions of

the body – such as a point on the hand that ‘brightens the eyes’ or one on the leg that ‘calms the mind’. Acupuncture clearly can have both local effects in tissues and more general effects on the brain ([Chapter 4](#)) or the autonomic system ([Chapter 6](#)), but the concept that remote effects are controlled by particular points seems far-fetched and without known physiological basis. However, some point combinations show greater effect on blood pressure than others ([Chapter 23](#)), so there is more to learn about the central connections of peripheral nerves.

## Clinical points

WMA emphasises the appropriate stimulation of nerve endings, usually in deep somatic tissues. TCA emphasises precise point location and point specificity, and sometimes uses the concept of points with the aim of treating the perceived underlying factors.

Treatment with WMA is based ideally on conventional diagnosis of the problem (but at least on an anatomical rationale) to determine where the stimulation must be given and how it must be given. Very often classical points will be used because they offer the most suitable locations, as the Chinese discovered.

## THE COMPLEXITY OF ACUPUNCTURE

Any person investigating acupuncture will be astonished by its complexity. For example, how can any treatment: (1) reduce acute postoperative pain now; (2) diminish symptoms of chronic painful and stiff knees for several weeks; (3) prevent episodes of migraine for several months; and (4) reduce nausea and vomiting after subsequent surgery or chemotherapy? Yet there is evidence for all these effects and mechanisms to explain most of them.

## Mechanisms

Needles can produce a wide range of neural effects in the spinal cord, brain stem, limbic system, hypothalamus and cortex ([Chapter 3](#)). Needles can alter perception, autonomic activity and immune responses. Needles also have marked local tissue effects. If there is a single principle for the effects of acupuncture, it is to restore the resting state, well exemplified by its activation of the ‘default mode’ of the brain ([Chapter 4](#)). These effects reduce the impact of chronic pain, a symptom that is increasingly understood ([Chapter 5](#)). Acupuncture also modulates the autonomic nervous system, thus having important influence on the internal organs ([Chapter 6](#)).

Now that the purely physical modes of action of acupuncture are clearly established, attention is being paid to mechanisms of its psychological components (discussed in [Chapter 7](#)). These can be expressed both as the ‘placebo response’ and as the ability of the psyche to modify the specific responses to the needle. The picture becomes almost impossibly complex, providing significant advantages for patients (but significant problems for research and for public understanding).

## Clinical approach

The section on clinical approaches illustrates a range of techniques for stimulating a response. The standard approaches are well established ([Chapter 7](#)), and parallel approaches emphasise identifying areas for treatment ([Chapter 8](#)), needling superficially ([Chapter 9](#)), stimulating reflexes through the auricle ([Chapter 10](#)) or adding electrical stimulation ([Chapter 11](#)). In many cases the patient or their carer can continue to use acupuncture away from the clinic ([Chapter 12](#)). Examples of ways in which acupuncture is integrated with other Western medicine are described in [Chapter 13](#). Underlying all these approaches is the need to ‘first do no harm’ ([Chapter 14](#)). Other forms of stimulation related to acupuncture are then described: TENS ([Chapter 15](#)) and laser ([Chapter 16](#)).

## Indications

This complexity of acupuncture mechanisms and approaches is reflected in the wide range of conditions for which acupuncture is used, described in the section on clinical use, from the pain clinic, through psychiatry and palliative care, to veterinary medicine.

This range of effects can be explained by acupuncture's known modes of action in pain pathways, the limbic system, the hypothalamus and the autonomic nervous system. Some enthusiasts see acupuncture as a profound and special system of treatment with the qualities of a panacea: we strongly disagree. Although there may be broad applications for individuals who are particularly sensitive to the effects of acupuncture, acupuncture should be seen as an adjunctive or complementary treatment and not as an alternative to more definitive conventional care.

There are, however, increasing numbers of specific areas where acupuncture may expect to be integrated with conventional care, and even first-line treatment. The best evidence exists for various pain conditions (pain clinic, [Chapter 19](#); surgical analgesia, [Chapter 20](#); rheumatology, [Chapter 35](#); and sports medicine, [Chapter 36](#)); for nausea and vomiting ([Chapter 22](#)) from various causes; and for chronic headache (neurology, [Chapter 24](#)). Evidence is accumulating for acupuncture's role in genitourinary medicine ([Chapter 27](#)), otorhinolaryngology ([Chapter 29](#)), gynaecology and infertility ([Chapter 32](#)) and functional disturbances of the gut viscera (gastroenterology, [Chapter 21](#)).

Formal evidence from rigorous RCTs has not yet convincingly supported clinical experience of acupuncture's value in aspects of other clinical areas, including cardiovascular medicine ([Chapter 23](#)), mental health ([Chapter 25](#)), drug dependence and obesity ([Chapter 26](#)), respiratory conditions ([Chapter 28](#)), eye conditions ([Chapter 30](#)), and skin conditions ([Chapter 31](#)). Whether this is because research has failed to reveal genuine effects, or because acupuncture only has context effects in these conditions, only time and further research will decide. What can be said is that, whatever its mechanisms, acupuncture provides many patients with real relief in fields as wide ranging as obstetrics ([Chapter 33](#)), cancer and palliative care ([Chapter 34](#)), primary care ([Chapter 37](#)), dentistry ([Chapter 38](#)) and veterinary medicine ([Chapter 39](#)).

## WMA: challenges

Acupuncture offers considerable benefits to patients (see [Box 1.1](#)), is popular and is supported by evidence shown in this book. Its disadvantages are clear but relatively minor – some patients are needle-shy and refuse it, and it is time-consuming to use, for example, in comparison with writing prescriptions. So why is it not universally accepted?

The main challenges that WMA faces are that acupuncture is perceived as implausible, that clinical responses are dismissed as placebo and that clinical research is seriously constrained. Underlying these challenges is its complexity, already discussed, and the disinclination of critics to engage fully with the necessary detail. Open minds are needed to extricate acupuncture from its traditional origins, and to consider seriously valid models of non-pharmacological research and medicine.

### BOX 1.1 ■ Attractions of Western medical acupuncture

- Is safe, effective and cost-effective
- Has a wide range of applications
- Benefits can be maintained with infrequent top-up treatments
- Treatment can in some cases be continued by the patients themselves
- Can be used when comorbidities are present
- Has few (if any) interactions with medications
- Is a useful adjunct to other physical interventions such as exercise
- Is based on science and has known modes of action
- Is easily learned and uses inexpensive equipment

## PLAUSIBILITY

The general public tends to equate ‘acupuncture’ with TCA, relying on explanations of ‘balancing Qi flow in meridians’. The concepts of balance, Qi flow and meridians are implausible if taken literally, given what we now know about the structure and function of the body. The use of traditional theory is particularly challenging (to put it mildly) to evidence-based medicine. WMA offers acceptable solutions, but until it becomes more widely understood, the rational arguments remain unheard, especially as its explanations are not simple and uni-dimensional but complex.

The most obsolete and inexcusable version of this scepticism is those commentators who take the attitude ‘It *can’t* work, so it *doesn’t* work.’ This is a simplistic denial of the principle exemplified by other significant medical discoveries which seemed implausible until mechanisms were discovered: WMA is to TCA just as digoxin is to the foxglove, or aspirin to willow bark. Acupuncture’s challenge is to get its explanations more widely read and understood.

Acupuncturists have a role in increasing the treatment’s acceptability, although some promote irrational ideas and make claims that stretch credibility: mechanisms demonstrated in the laboratory may not be relevant to clinical care, and not every response hailed by an acupuncturist is due to needling. This book attempts to balance an open-minded approach with rigorous research.

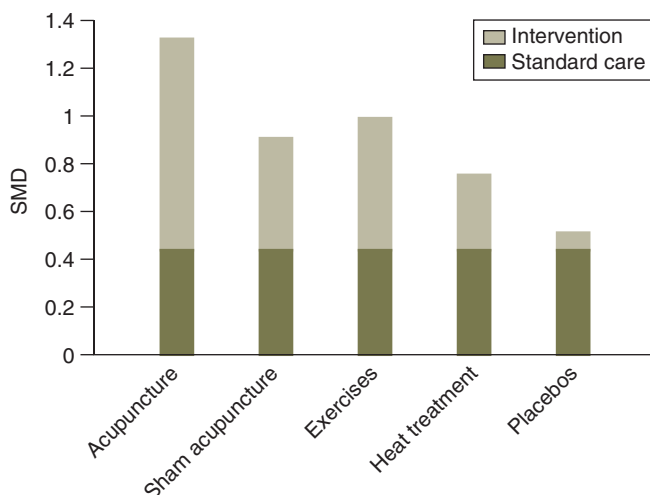
## PATIENT RESPONSES TO ACUPUNCTURE

There is a considerable gap between the views of some in the scientific community who dismiss acupuncture as no more than placebo, and practitioners who have confidence in acupuncture because they see patients respond in ways that are not explained by placebo. There are undoubtedly individual responses that are unpredictable and spurious, but they are the exception not the rule.

Every efficacious medical intervention generates a placebo response (also referred to as non-specific effects, or context effects) as well as specific effects. The nonspecific effects of acupuncture are larger than the total effects of other interventions: a network meta-analysis of physical treatments for knee osteoarthritis pain compared with usual care showed acupuncture clearly superior to all (Fig. 1.1; Corbett et al., 2013). Sham acupuncture is more effective for osteoarthritis pain than heat treatment – yet heat treatment is recommended while acupuncture is not (NICE (National Institute for Health and Care Excellence), 2014). These large nonspecific effects of acupuncture can be larger than the specific effects of needling; that is not a problem in clinical practice or in head-to-head studies comparing acupuncture with other therapies, but does create a problem for decision-makers using an uncompromisingly narrow evidence-based medicine approach.

Sometimes the patient’s response to acupuncture seems like ‘magic’ in either its suddenness or its unpredictability. Grateful patients are likely to report such a response enthusiastically, offering a target for sceptics to easily dismiss acupuncture as a ‘placebo response’. This judgement is then (lazily) applied to the whole of acupuncture. Much less newsworthy is the more common response – predictable, steady benefit over several treatments. Magical responses benefit the patient, but are atypical and unpredictable so cannot easily be investigated. This book sticks to the scientific approach and steers clear of ‘magical thinking’.

The undoubted contribution of the placebo response to acupuncture is a problem – making uncontrolled clinical observations unreliable and stressing reliance on high-quality controlled studies. The placebo response comes to dominate the acupuncture research agenda, and causes major problems in both designing and interpreting clinical trials – see Chapters 17 and 18.



**Figure 1.1** Network meta-analysis comparing physical interventions for osteoarthritis knee pain. Explanation: Overall effects of various interventions for knee osteoarthritis pain (light green) in comparison with standard care (dark green). SMD, standardised mean difference (*Reproduced from Corbett, M.S., Rice, S.J.C., Madurasinghe, V., et al., 2013. Acupuncture and other physical treatments for the relief of pain due to osteoarthritis of the knee: network meta-analysis. Osteoarthr. Cartil. 21, 1290–1298.*)

## PROBLEMS IN ACUPUNCTURE RESEARCH

The clinical effects of acupuncture are obvious, so one might expect them to be easy to demonstrate in clinical trials. They are, when compared with the effects of the waiting list, usual care or even other treatments. The problem comes when trying to compare acupuncture to ‘placebo’: placebo acupuncture appears to be simple to arrange for TCA with its belief in point specificity, but is difficult or even impossible to arrange for WMA.

### The ‘missing placebo’

In traditional theory, acupuncture needles have to be inserted into acupuncture points; therefore placing the needle anywhere outside the point constitutes ‘placebo acupuncture’. Readers of this book probably know that nerves exist almost everywhere in the body, so naturally needles outside the point have similar effects to those in the point ([Chapter 17](#)). Every attempt to devise an inactive ‘placebo needle’ cannot avoid stimulating the nervous system to an extent that is not much different from the specific effects of the needles ([MacPherson et al., 2014](#)). Thus it has proved extremely difficult to demonstrate acupuncture’s specific effects and large studies are needed.

This ‘missing placebo’ problem is not unique to acupuncture, but shared by other physical interventions (exercise, manipulation, surgery, acupuncture) and psychological ones (cognitive behavioural therapy, counselling). Extensive contact between practitioner and patient is inherent in these treatments. In fact, in the whole field of research into medical treatments, pharmaceutical research is the exception in having a simple, inactive placebo readily available. The elegant simplicity of the placebo model of clinical trials allows double-blinding and so dominates decision-making in healthcare policy. Placebo-controlled trials of acupuncture are impossible, so evidence on acupuncture is inevitably open to the criticism that it is affected by bias. But policy has to be made, so it should be based on the best available other evidence.

Other decision-makers – physicians and patients – are more interested in how acupuncture treatment compares with best standard treatment, and here there is plenty of high-quality evidence with positive results.

### Other constraints

A major obstacle to acceptance of WMA is that the great majority of clinical research has been based on TCM concepts of point specificity, not Western concepts of neural stimulation. The majority of studies claiming to be placebo controlled actually compare real acupuncture with a weaker dose.

Acupuncture is not widely accepted in the mainstream, so research is not well resourced. Phase I trials are rare, so we have no systematic exploration of indications for treatment, or of the optimal dose/schedule of acupuncture. Research is based on clinical tradition rather than controlled observation. This problem is of course circular: acceptance would bring resources for studies, and more studies would bring greater acceptance.

Many clinical studies are performed by isolated clinicians enthused by clinical success without adequate access to experienced research support, though there are obvious exceptions. Studies are commonly undersized and inadequately designed, producing ‘inconclusive’ answers and correspondingly negative public impact.

## WMA: accumulating evidence

It is an accepted truth that patients’ needs are best served by evidence-based rather than ‘eminence-based’ medicine. Acupuncture research, at least for some conditions, has overcome some design problems and achieved the volume required to provide reliable evidence. This research is broadly of two types: comparison with sham, and comparison with other interventions.

### PROOF OF PRINCIPLE

Comparing real acupuncture with sham acupuncture tests whether needles result in net benefit – or net harm for that matter. This addresses the question of whether acupuncture has specific effects, an important test of proof of principle since it seems widely believed that interventions that do not have specific effects should not be funded from public sources.

The evidence that acupuncture needles have specific effects is overwhelming. In terms of physiological effects, reviews of laboratory studies of acupuncture convincingly show analgesic effects (Zhao, 2008 and Chapter 2). In imaging studies in humans, real needling produces effects that are clearly different from sham needling (Huang et al., 2012 and Chapter 4). Turning to clinical benefits, the highest-quality evidence of acupuncture using individual patient data from only rigorous studies finds it superior to sham for several chronic pain conditions (Vickers et al., 2012 and Chapter 19). Even more convincingly, the closest thing to a double-blind study is in postoperative pain where patients, carers and assessors can all be masked. Even under these strict conditions, acupuncture shows a significantly greater pain control than sham acupuncture, both by dose of analgesic drug and by pain threshold (Ntritsou et al., 2014 and Chapter 20).

### EVIDENCE OF CLINICAL BENEFIT

Evidence that acupuncture ‘can’ work in principle does not itself mean that it benefits patients in practice. Acupuncture’s place in healthcare is decided by clinical trials that compare acupuncture with other treatments that are available for the condition – for effectiveness, for cost-effectiveness and for safety.

Throughout this book we shall see convincing evidence of acupuncture's effectiveness against no acupuncture, the clearest example being the highest-quality evidence of acupuncture for chronic pain (Vickers et al., 2012). But it must also be compared with other available treatments, for example, using network meta-analysis. For knee osteoarthritis, a condition where plentiful evidence exists, acupuncture proved superior to all other available conservative non-pharmacological therapies (Corbett et al., 2013).

This rigorous evidence from trials has repeatedly confirmed clinical impressions from careful observation in clinical situations where acupuncture is integrated with other forms of conventional care (Chapter 13). It seems that decision-makers at the local level, in near contact with patients, are willing to base decisions on the 'softer' evidence from audits and clinic reports and patient testimony, when this is consistent and credible, while policy-makers at the central level remain unconvinced even by scientifically robust data.

Acupuncture's safety record now provides plentiful evidence that it is safe in the hands of trained practitioners (Chapter 14). Finally, acupuncture has often been proved cost-effective by the usual healthcare standards, for most conditions including back pain and osteoarthritis (Chapter 19) though not for all conditions, e.g. allergic rhinitis (Chapter 29).

## WMA: increasing acceptance

Acupuncture is increasingly accepted and integrated locally, and recommended in some health policy guidelines (examples from the UK include NICE CG88, 2009; NICE CG150, 2012; SIGN, 2013). However, other guidelines still do not recommend acupuncture (for example, NICE CG177, 2014), basing that decision on the comparison with sham acupuncture. This seems to risk putting statistical principle before patient benefit, and we believe that patients are not best served by being denied a treatment that is established as effective in relation to other available treatments, even though not established 'beyond all doubt' as effective against sham. Because of the constraints on gold standard, placebo-controlled trials of acupuncture, it has proved remarkably difficult to provide definitive evidence on acupuncture whose interpretation is beyond debate.

Acupuncturists still face the exciting challenge of convincing sceptics that the unlikely process of inserting fine, solid needles into the body can help a medical condition. We believe the evidence in this book will support them in meeting the challenge as it provides a clear exposition of the range of mechanisms activated by acupuncture, together with realistic surveys of the genuine benefits of acupuncture, the identification of unfounded claims and useful details on clinical approaches. There is inevitably some overlap between authors, and yet not all authors hold exactly the same views. We hope that readers will find the approach stimulating and will encourage further debate and the acquisition of more relevant clinical evidence.

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# The history of medical acupuncture

A. Campbell

## CHAPTER OUTLINE

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## Introduction

For most people, ‘acupuncture’ connotes an ancient Chinese treatment that uses needles inserted at specific points which are supposed to lie on so-called meridians. The earliest Chinese references to this form of therapy go back 2000 years, but the name by which we know it is of Western origin, being derived from the Latin for ‘needle’ and ‘piercing’. This chapter is concerned with modern medical acupuncture, which means that it refers to how acupuncture has developed in the West in the last 300 years. In outline, this has occurred in four stages. I first summarise these and then explain them in more detail.

### Stage 1 (seventeenth and eighteenth centuries)

First inklings reach the West, culminating in the publication of *De Acupunctura* in 1683 by the Dutch physician Willem ten Rhijne.

### Stage 2 (nineteenth century)

Physicians in France and Germany practise acupuncture but with little reference to its Chinese roots. In Britain acupuncture is popular in the 1820s but later largely disappears.

### Stage 3 (first half of twentieth century)

Widespread infusion of traditional ideas into acupuncture as practised in mainland Europe.

### Stage 4 (second half of twentieth century to present day)

Interest in acupuncture is revived in Britain by Felix Mann, who interprets the treatment in modern terms. Increasing acceptance of this form of acupuncture by health professionals leads to research in acupuncture in many countries and a better understanding of acupuncture mechanisms.

## Stage 1: seventeenth and eighteenth centuries

Although scattered references to acupuncture were made by missionaries to China in the seventeenth century, the first detailed description to reach the West appeared in 1683, thanks to a Dutch physician, Willem ten Rhijne (Fig. 2.1), who worked for the Dutch East India Company and saw the treatment being used by Japanese physicians in Japan and Java.

On his return he wrote, in Latin, an account of his experience, *De Acupunctura* (Fig. 2.1) which he included in his *Dissertation on Arthritis*. The term ‘acupuncture’ was already in use but had hitherto been applied to the insertion of needles to drain fluid accumulation due to oedema or ascites (Barnes, 2005.). A few decades later ten Rhijne’s successor in Java, Englebert Kaempfer, contributed further though limited information.

The charts which ten Rhijne obtained – with some difficulty – showed acupuncture channels, but their significance was not understood either by ten Rhijne himself or by those who read his account (Fig. 2.2). Western physicians remarked on the neglect of internal anatomy in the charts. It was not only the internal organs that were missing. The lines that meandered over the depiction of the body were assumed to indicate blood vessels but they bore no relation to the blood vessels known to Western anatomists. This was taken to be evidence of ignorance. And there was no depiction of muscles – another striking omission (Fig. 2.3). In fact, Western emphasis on the muscles, which went back ultimately to classical Greek models, was in its own



Figure 2.1 Willem ten Rhijne.

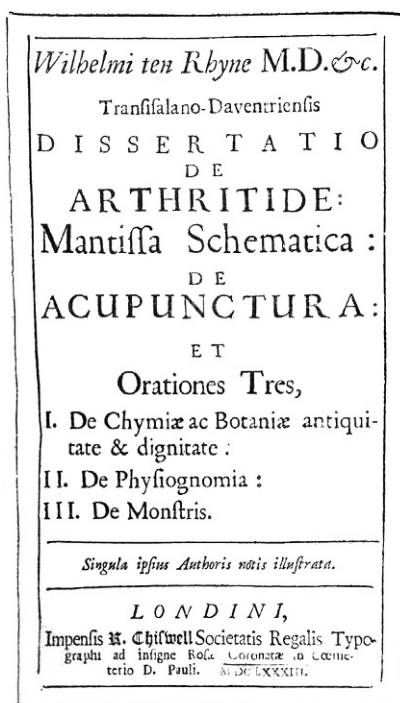


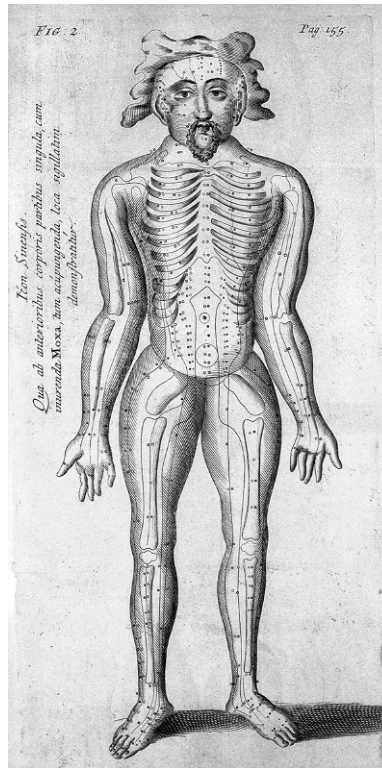
Figure 2.2 Frontispiece of Willem ten Rhijne's *De Acupunctura*.

way as much a convention as was the Japanese and Chinese neglect of them (Kuriyama, 1999), but it did reflect an important difference in how Western and Eastern physicians thought about the body. Not until the twentieth century did the Chinese recognise the existence and function of muscles (Kuriyama, 1999).

In spite of such criticisms a number of eminent eighteenth-century medical writers quoted from ten Rhine's and Kaempfer's works and reproduced ten Rhijne's illustrations, but there seems to have been little if any attempt to apply acupuncture in practice in the West at this time. Indeed acupuncture was in decline in China itself in the eighteenth century – one Chinese physician called it a lost art (Barnes, 2005). Nevertheless attempts were made to explain how it might work, and one writer at least was remarkably prescient. In 1755 Gerard van Swieten, personal physician to the Austrian Empress Maria Teresa, postulated a neurophysiological explanation for acupuncture: 'It would be an extraordinarily useful enterprise if someone would take the trouble to note and investigate the marvellous communion which the nerves have with one another, and at what point certain nerves lie which when stimulated can calm the pain at different points' (Bivins, 2000). This is essentially the explanation we accept today.

## Stage 2: nineteenth century

Not until the early nineteenth century do we find physicians in France and Germany actually trying out acupuncture. Electricity was just beginning to be understood at this time and the connection between electricity and nerve transmission was starting to be recognised. It seemed natural



**Figure 2.3** Chinese chart of meridians and points. (Reproduced by Willem ten Rhijne.)

to many physicians to explain acupuncture in electrical terms and electrical stimulation of the needles was tried by Louis Berlioz, the father of the composer Hector Berlioz. He was probably the first physician to use acupuncture in France. His first patient, whom he describes as a charming and attractive blonde aged 24, actually administered the treatment to herself under his supervision, with very good effect. Berlioz later made the important observation that the results were better when the needles produced little or no pain (Tailleux, 1986).

In Britain scattered references to ‘acupuncturation’ began to appear in the early years of the nineteenth century, but they attracted little attention until, in 1821, a young surgeon, John Morss Churchill, published the first monograph on the subject in English. In *A Treatise on Acupuncturation* he cited the French research, including that of Berlioz, but had little to say about the Chinese origins of acupuncture, although, curiously, he made a connection with Indian practice (Churchill, 1821). He was unable to offer an explanation for how the treatment might work although from his own experience he was sure that it did.

Churchill’s monograph was well received and a number of doctors took up the practice of acupuncture. *The Lancet* endorsed it in 1826, and although there were critics, many who tried it were impressed, especially by the rapidity of response. Acupuncture was generally considered to be safe, although the need for a good knowledge of anatomy was recognised: Churchill thought that acupuncture should be performed by surgeons. (This may be connected with the fact that surgery had only recently achieved academic recognition in Britain on a par with medicine.) Churchill cites French physicians who used long (3-in.) needles and thought needling the abdominal viscera,

heart and brain posed no real risk, but Churchill himself did not advocate this. The needles would presumably not have been sterilised at this time, since Joseph Lister's introduction of surgical antisepsis did not happen until the second half of the century, but we do not hear of complications that sound like infection.

The distinction between acupuncture and other surgical procedures such as blood-letting was not always clear, and some of those who took up the practice used it in rather odd ways: one, for example, needled a strangulated hernia and apparently reduced it successfully. Acupuncture was widely used to treat sciatica, as might be expected; the technique consisted of deliberately needling the sciatic nerve on the grounds that post mortem the nerve had been found to be red and swollen in people who had died with sciatica and that therefore acupuncture worked by letting the fluid out.

Churchill's original description contained a few cases of his own together with some from other sources; in a follow-up to his monograph in 1828 he published a number of new cases (Churchill, 1828). He describes two men with severe acute back pain who were immediately relieved by the insertion of needles in the lumbar muscles, and two women with 'rheumatalgia' who failed to respond adequately to medical treatment but were cured by the insertion of needles in the intercostal muscles.

The initial enthusiasm for acupuncture among British doctors did not last. In part this was because no one, including Churchill, could suggest how it might work. We hear little about the subject in Britain after 1828 although it was probably still being used to some extent, because acupuncture needles continued to be advertised by suppliers of medical equipment in London (Barnes, 2005). And it was certainly practised at two centres – the Leeds Infirmary and University College Hospital in London – until at least the 1870s.

The acupuncture in vogue in Europe in the nineteenth century was set in the context of the medical knowledge of the day and had little connection with traditional Chinese acupuncture beyond the use of needles. Then, as now, its main application was to musculoskeletal pain. It therefore had a lot in common with today's medical acupuncture although there were also differences, notably the fact that referred pain was not used as a guide to treatment; the needles were merely inserted at the site of pain. The duration of needling varied, but the needles were not stimulated manually, being simply left in place for a time that varied between less than a minute and several hours or even days. Relief of pain was often immediate although the treatment itself could be painful; indeed, unlike the French, some British practitioners insisted that acupuncture had to hurt to be effective.

### Stage 3: 1900–60

Acupuncture continued to be used in France in the first half of the twentieth century to the occasional bewilderment of British medical visitors, for it was now almost unknown in Britain. But its character changed; it moved away from conventional science and became more traditional. This somewhat surprising development was due to a Frenchman, George Soulié de Morant (1878–1955), who had gone to China in 1901 to work in a bank. He became deeply interested in Chinese medicine, especially acupuncture. On his return to France he practised acupuncture and taught it both to doctors and to people without medical training. He also translated a number of Chinese medical texts into French.

The view of acupuncture popularised by Soulié de Morant is still influential today. In particular, his rendering of *qi* as 'energy' and his use of the term 'meridian' to refer to the acupuncture channels have been widely adopted. He apparently believed that his approach would make acupuncture more acceptable to Western scientists, but if anything it has had the opposite effect (Kendall, 2008). Nevertheless these ideas became widespread, not only in France but also in other European countries and the USA, where they were increasingly taken up by health

professionals interested in acupuncture. In Britain, meanwhile, acupuncture had more or less disappeared, at least among health professionals, so Soulié de Morant's views had little impact here.

## Stage 4: 1960 to the present

Any British doctor who wanted to study acupuncture in the first half of the twentieth century needed to go abroad, since nothing was available at home. One who did so in the 1950s was Dr Felix Mann (1931–2014), who was to have a decisive influence on the course of acupuncture in Britain. He studied with Dr Anton Strohl in Munich, Professor Johannes Bischko in Vienna and Dr van Nyha at Montpellier (Baldry, 2005). Later he sought the help of sinologists and studied Chinese in order to be able to read the ancient and modern texts. He also visited China. Throughout this period he was learning traditional Chinese acupuncture since, as he explained later, nothing else was then available (Fig. 2.4).

On his return to London in 1959 he set up an acupuncture practice in the West End – a brave step at the time, since acupuncture was almost unknown in Britain. Encouraged by the good results he was soon getting he persevered and also started to teach acupuncture to doctors, although initially only a few attended. Between 1959 and 1964 he published four books on acupuncture. These were intended for Western practitioners and were based on modern disease terminology, but gave indications for treatment in terms of traditional points.

In the mid-1960s a radical change came over Mann's thinking. He always reflected critically on what he was doing, and some of his observations led him to doubt the validity of the traditional view of acupuncture that he had been taught. He experimented by putting needles in 'incorrect' places and found that the results were as good as when he used the prescribed sites. He found that needling did not have to be nearly as precise as the traditionalists believed. It was, he decided, better to think in terms of areas rather than points, and the areas could be quite large; in some patients anywhere in the relevant limb might work, with no need for further precision. As a result of his experiments he came to the conviction that acupuncture points and 'meridians' do not exist, at least as traditionally conceived. Eventually he developed his own version of acupuncture, which



**Figure 2.4** Dr Felix Mann (1931–2014) who brought acupuncture into the scientific era by stating 'Acupuncture points don't exist, meridians don't exist'.

was essentially a modern one based on the idea that acupuncture works by modifying the action of the nervous system (Mann, 2000).

Once freed from the conceptual constraints of the traditional system, Mann went on to make a number of very important contributions to acupuncture. One was his recognition of a group of patients – ‘strong reactors’ – in whom acupuncture had a particularly dramatic effect. They required less intensive treatment than average and, if treated gently, they responded exceptionally well: disorders for which acupuncture usually failed could sometimes be helped in a strong reactor. For Mann, treatment intensity (number of needles, duration of needling, amount of manual stimulation) was always a critical factor, and over the years he tended to use more and more gentle stimulation for nearly everybody. The existence of a strong reactor category is now widely accepted in modern medical acupuncture.

Mann was always looking for new ways to treat patients, and he constantly tried out different techniques in an attempt to get better results. One of his most important innovations was periosteal acupuncture. He used this to treat intrinsic joint pain and also more generally, because it seemed to have particularly wide-ranging effects. For example, he said that needling the articular pillar in the neck could influence practically any disorder in the upper half of the body; similarly, needling the pelvic periosteum in the region of the sacroiliac joint was useful for referred pain anywhere in the lower limbs.

Mann frequently lectured abroad in many countries and reported that his views had a mixed reception. At home the number of doctors attending his training courses increased in the 1970s, and probably most doctors who learnt acupuncture in those years did so from him. They constituted an informal medical acupuncture society which was the forerunner of the British Medical Acupuncture Society (Baldry, 2005), founded in 1980 with Mann as its first President. It now has over 2000 members.

Mann’s contributions to acupuncture are many, but the most important is the major change he brought about in how many Western health professionals regard the subject. Modern science owes its origin to a decisive shift in thinking that began in Europe some 300 years ago in the Enlightenment. The new attitude is essentially sceptical and iconoclastic; it is based on a refusal to accept the authority of tradition and a willingness to question everything. Traditional acupuncture, in contrast, belongs to the pre-Enlightenment era and is characterised by reverence for tradition and a conviction that everything that matters was discovered in the remote past. By questioning the tradition and by seeking for neurophysiological explanations for how the effects of needling are produced, Mann may be said to have laid the foundation of post-Enlightenment acupuncture.

## THE IMPACT OF NEW DISCOVERIES

Acupuncture in the late 1960s was still regarded by most people in Britain, and certainly by most health professionals, as exotic and a form of ‘fringe’ or alternative medicine. But matters began to change in the 1970s, for several reasons. One was President Nixon’s visit to China in 1972. James Reston, a journalist accompanying the mission, developed appendicitis and received acupuncture postoperatively to provide relief from pain and paralytic ileus. Subsequently Western surgeons visited China and saw patients apparently having acupuncture analgesia for major operations. Acupuncture achieved considerable prominence as a result of these events.

Two scientific developments at about this time helped to make acupuncture appear more comprehensible. A few years earlier, in 1965, Melzack and Wall had put forward the gate control theory of pain. Their understanding of pain perception as based on a balance between excitation and inhibition provided an explanation for phenomena such as the absence of pain reported by people who received injuries in sport or battle, and their ideas had a profound effect on the modern understanding of pain physiology. It also appeared to offer a mechanism by which acupuncture might work; Melzack and Wall both commented on this (Melzack and Wall, 1965).

The other important development was the discovery of the endogenous opioids in 1974. The possible relevance of these to acupuncture was easy to see, and a lot of research was carried out in animals and humans. High levels of beta-endorphin were found in human cerebrospinal fluid after acupuncture for pain, for example, and the pain-relieving effect of acupuncture could be blocked by naloxone (Clement-Jones et al., 1980). Although it now appears that endorphin release is only part of the story, explanations of this kind helped to make acupuncture more acceptable to Western practitioners. Research studies like these were starting to provide a basis for claiming that acupuncture had demonstrable physiological effects, and the technique began to be more widely used in British hospitals and pain clinics. Researchers in other countries have continued to expand the scientific base of acupuncture; among those who have contributed important insights are Lundeberg and Andersson in Sweden, Han in China and Sato in Japan.

## MYOFASCIAL TRIGGER POINTS AND ACUPUNCTURE

Another important element in the story of twentieth-century acupuncture came from work, principally by Janet Travell and David Simons, on myofascial pain. This followed on from research on by Kellgren in the 1930s (Baldry, 2005). He injected hypertonic saline into the muscles of volunteers and found radiation to distant areas. He also applied this therapeutically, noting that injecting local anaesthetic into the sites from which pain was referred could alleviate pre-existing musculoskeletal pain. He carried out this research at University College Hospital in London, at the behest of Sir Thomas Lewis, director of clinical research at the hospital. It is conceivable that it was echoes of the earlier use of acupuncture there in the previous century that prompted Lewis's interest in the subject, although no explicit connection with acupuncture was made at this time.

Travell, later joined by Simons, took up this idea and went on to develop the concept of the myofascial pain syndrome (Travell and Simons, 1999). Tender areas, mainly in muscles but also in other tissues such as the attachment of ligaments, could refer pain and other sensations to distant areas. These myofascial trigger points (MTrPs), as they were called, were postulated to be the cause of much musculoskeletal pain. They could be activated in various ways, for example by overuse, and then could persist for a long time. For treatment Travell and Simons mainly used a cooling spray followed by stretching, but they also injected local anaesthetic into the MTrPs. Some practitioners took the logical next step of simply inserting the needle without injecting anything – so-called dry needling, which is best regarded as simply another name for modern medical acupuncture.

Most modern medical practitioners now use MTrPs at least to some extent, and some more or less equate modern acupuncture with this kind of treatment. Baldry is prominent in this respect; he finds that there is a lot of similarity in the locations of classic acupuncture points and those of trigger points recorded in the Western literature, while 'Ah Shi' points (sites that become tender in disease) and trigger points seem to be the same thing (Baldry, 1998). Another practitioner who takes a broadly similar approach is Macdonald (1991).

## THE PRESENT SITUATION OF ACUPUNCTURE

The second half of the twentieth century saw a large increase in the practice of traditional acupuncture in Western countries, mainly by people without a background in conventional medicine. This trend accelerated later as the Chinese began to offer training to Westerners, initially in China but later abroad. These developments did not take place in isolation but were part of a more widespread acceptance of unconventional therapies both by patients and by conventional practitioners. Today both modern and traditional versions of acupuncture are in use in many Western countries. But rather than a rigid division into traditional and modern versions, what

we see is more like a spectrum. Some practitioners wish to adhere as closely as possible to traditional ideas, although this is a minority position among health professionals. But even those who regard themselves as modernists may incorporate some elements of the traditional concepts into a predominantly modern approach. They may, for example, use classic points preferentially, while assuming that they have some physiological basis that makes sense in a modern context; or they may interpret the 'meridians' to mean commonly found patterns of pain radiation. But other practitioners ignore the traditional ideas almost completely.

Acupuncture refers, by definition, to the insertion of needles, which makes it difficult to know how to classify treatments such as laser 'acupuncture' which do not use needles but which have developed as offshoots from acupuncture. Transcutaneous electrical nerve stimulation via conducting pads is another non-needle development. But even if we confine ourselves to needle therapy the twentieth century has seen the introduction (or reintroduction) of new kinds of acupuncture. The nineteenth-century application of electricity to the needles continues today and is quite widely used. Traditional acupuncture consisted of inserting needles at various sites in the whole body, but a number of new systems of acupuncture make use of localised body maps. The best-known of these is Nogier's system of ear acupuncture (auriculotherapy) (Hsü, 1992), but others exist, such as Yamamoto's scalp acupuncture (Umlauf, 1991).

## THE FUTURE OF ACUPUNCTURE IN THE WEST

Acupuncture, at least the modern medical variety, is probably the form of unconventional treatment that has achieved the greatest degree of medical acceptance. This is largely because a substantial body of research exists to show that insertion of needles has demonstrable physiological effects. This provides a basis for thinking that acupuncture is a real neurophysiological treatment. The needles do something. But it has proved more difficult to demonstrate that these effects are specific either to the exact site of needle insertion or, indeed, to the use of needles as opposed to other forms of cutaneous or muscular stimulation. It may be, therefore, that acupuncture is one among a group of therapies that all work in much the same way, perhaps via a final common path that includes the limbic system (Campbell, 1999).

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## ***Mechanisms of action***

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## Peripheral components of acupuncture stimulation – their contribution to the specific clinical effects of acupuncture

T. Lundeberg ■ I. Lund

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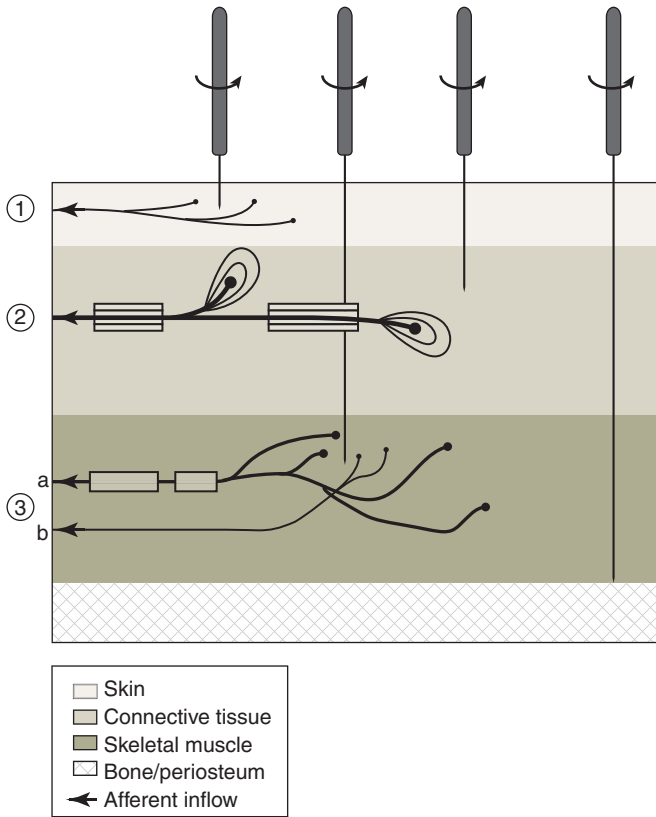
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## ABBREVIATIONS

5-HT	serotonin
ACh	acetylcholine
AMP	adenosine 5'-monophosphate
AMPK	AMP-activated protein kinase
ATP	adenosine 5'-triphosphate
BDNF	brain-derived neurotrophic factor
Ca <sup>2+</sup>	calcium ion
cAMP	cyclic adenosine 5'-monophosphate
CGRP	calcitonin gene related peptide
CNS	central nervous system
CT	C tactile
CXC	family of chemokines
DMN	default mode network
DNA	deoxyribonucleic acid
DRG	dorsal root ganglion
DRR	dorsal root reflexes
eNOS	endothelial nitric oxide synthase
EPO	erythropoietin
FGF-2	fibroblast growth factor-2
FSTL	follicle-stimulating-like
GABA	gamma amino butyric acid
H <sup>+</sup>	hydrogen ion
HPA	hypothalamus-pituitary-adrenal
IL	interleukin
IML	intermediolateral column
K <sup>+</sup>	potassium ion
NE	norepinephrine
NGF	nerve growth factor
NO	nitric oxide
PAG	periaqueductal grey
PG	prostaglandin
TGF- $\beta$	transforming growth factor beta
TNF	tumour necrosis factor

## Introduction

The content of this chapter is mainly focused on describing the possible effects of acupuncture stimulation on the body's peripheral tissue and organs, i.e. the peripheral components of acupuncture stimulation, and the consequent effects on physiological function. In general, clinical effects following acupuncture stimulation can be described as deriving from physiological and/or psychological mechanisms where the needle stimulation could represent the artificial activation of systems obtained by natural biological effects in functional situations. The sensory stimulation that is induced by acupuncture, i.e. activation of receptors and or nerve fibres in the stimulated tissue,



**Figure 3.1** Tissue layers that may be directly or indirectly influenced by the needling procedure. **(1)** CT afferent, mediates touch from naked nerve endings. **(2)** Aβ afferent; mediates pressure, touch or vibration from encapsulated nerve endings. **(3a)** Aδ afferent; mediate hard pressure from naked nerve endings (ergo-receptors). **(3b)** C afferent; mediates nociception from naked nerve endings.

seem to elicit similar effects in man and other mammals, suggesting that it produces fundamental physiological changes. Hypothetically, acupuncture's physiological counterpart of such effects on certain organ functions lies in physical exercise with strong muscle contractions.

During acupuncture stimulation sharp, thin needles are inserted into specific 'acupuncture points' on the body whose location may be defined by surface anatomical landmarks. Histological studies have revealed that many acupuncture points have dense innervation, and are often located in direct relation to skeletal muscles, to connective tissue, as well as to cells with neuro-immune-modulatory role (Li et al., 2004; Fig. 3.1).

## Peripheral components of acupuncture stimulation – neural modulation

### THE PERIPHERAL SENSORY RECEPTORS

Acupuncture stimulation is associated with the activation of different sensory receptors, i.e. the terminal of the spinal dorsal root ganglion (DRG) neuron or trigeminal sensory neuron, in the skin and deeper tissues. Their properties and the corresponding sensation they give rise to, that

may be activated during acupuncture and moxibustion, include five major modalities (Kandel et al., 2013; Olausson et al., 2002, 2010; Schmelz et al., 1997; Sengupta and Garrity, 2013):

1. Mechanoreception (discriminative touch, size, shape, texture and movement)
2. Mechanoreception/proprioception (static position and movement)
3. Thermoreception (warmth/cold)
4. Nociception (pain)
5. Itch (itch)

The appearance of peripheral sensory receptors are of two types:

1. *Encapsulated* – nerve endings ‘covered’, often by connective tissue – mediating touch, pressure, vibration and proprioception
2. *Bare* nerve endings – nerve endings that end blind in peripheral tissue – mediating nociception/pain, itch, ‘emotional touch’ by gentle stroking and thermal sensations.

**Mechanoreceptors: cutaneous and subcutaneous**

Five major types of mechanoreceptors have been identified in glabrous (hairless) skin. Two of these are of the encapsulated type and are located in the superficial layers of the skin: Meissner's corpuscle and the Merkel disc receptor. The other two receptors, the Pacinian corpuscle and the Ruffini ending, also encapsulated, are found in the subcutaneous and deeper tissue layers (including between layers of muscle and on interosseous membranes). Similar types of mechanoreceptor are found in the hairy skin that covers most of the body surface including the hair follicles that respond to hair displacement. The fifth major type of mechanoreceptor is the bare nerve ending responding to stroking of the hairy skin.

**Mechanoreceptors: tendon, joints and skeletal muscle**

Four different types of mechanoreceptor are found in skeletal muscles, tendons and joint structures. Their main task is to give rise to the sense of movement and position of one's own limbs and body (proprioception), and sense of speed and direction of limb movement, and also to enable maintenance of an upright position (postural information) and manipulation of objects (Table 3.1).

Possibly, activation of these receptors by acupuncture combined with exercise in patients with neurodegenerative diseases may enhance the therapeutic outcome. Furthermore, many of the effects of mobilisation and or manipulation therapeutic techniques may be explained in terms of stimulation of these muscle and joint afferents.

Ergo-receptors are activated by hard pressure during muscle contraction (Kniffki et al., 1981) and also probably by acupuncture, when the sensation of *de qi* is evoked. It has therefore been suggested that the physiological counterpart to acupuncture is exercise (Andersson and Lundeborg, 1995). However, the ergo-receptors can also respond to metabolic stimuli of released H<sup>+</sup>, lactate or K<sup>+</sup> ions, i.e. acting as ‘metabolic chemoreceptor’. One of the neurotransmitters found in the ergo-receptors and also in a subgroup of afferent nerve fibres, the Aδ fibres, is calcitonin gene related peptide (CGRP) that could be released after muscle activity and acupuncture stimulation (Jansen et al., 1989; Shinbara et al., 2013). CGRP is a potent vasodilator of the capillary bed and restores

TABLE 3.1 ■ Mechanoreceptors in muscles, tendons and joint structures

Type of receptor	Stimulus for response
Muscle spindle receptors	Stretch of the muscle
Ergo-receptors	Pressure and tension (hard pressure during muscle contraction)
Golgi tendon organs	Contractile force exerted by the muscle
Joint capsule receptors	Flexion, extension and rotation of the joints

muscle blood flow during ischemic condition throughout and after exercise or static muscle load, serving as a part of a local auto regulatory mechanism. Also, CGRP may have a trophic effect on the endothelial cells acting as a growth factor, thereby contributing to angiogenesis.

**Mechanoreceptors: visceral organs**

Conscious sensations are not generally experienced from the visceral organs despite the fact that they are innervated by DRG neurons with free nerve endings, similar to mechanical nociceptors in the skin. The visceral mechanoreceptors are, however, sensitive to distension and stretching of visceral muscle, which may evoke sensations of pain. Chemosensitive nerve endings on the other hand play an important role in monitoring the visceral function and provide the afferent limb for many autonomic reflexes, both sympathetic and parasympathetic. The skin of the frontal part of the body overlying the visceral organs may be more densely innervated than that of the back of the body. This could be one reason why needling the front rather than the back may evoke stronger somato-visceral reflex responses.

**Thermoreceptors**

Four types of thermal sensations have been detected: cold, coolness, warmth and heat. The sensations are transmitted by thermal receptors whose firing is modulated as a function of temperature. A skin temperature of 34°C, a temperature neutral zone, is perceived as neither warm nor cold. Interestingly, cool receptors fire at skin temperatures of 18–25°C, whereas warmth receptors are most active at 45°C but stop firing at 50°C. Above or below these temperatures the sensation of heat or cold pain is perceived and transmitted by activity in the hot or cold receptors. It is likely that warm and/or hot receptors are activated during moxibustion, shock wave, high-energy laser and other modalities of therapeutic warmth/heat stimulation.

**Nociceptors**

Nociceptors are the receptors that selectively respond to nociceptive stimulation of peripheral tissue, as mentioned earlier, leading to perceived pain under certain circumstances. Pain is sometimes perceived in the absence of this activity but could then be due to sensitization processes in higher brain structures. Several classes of nociceptor have been distinguished and may be defined on the basis of their responses to different types of stimulus (Table 3.2).

The polymodal nociceptors are the most common class of nociceptor. During intense acupuncture stimulation, acupressure (painful) or strong massage, mechanical nociceptors may be

**TABLE 3.2 ■ Different classes of peripheral sensory receptors transmitting nociceptive signals, nociceptors, classified on type of stimulus**

Class of nociceptor	Stimulus/stimuli for activation
Mechanical nociceptors	Strong mechanical (painful) stimulus such as by sharp objects that penetrate the skin
Thermal nociceptors	Temperatures >45°C or <10°C activating heat and cold nociceptors
Chemical nociceptors	Chemicals such as bradykinin, substance P (SP), K <sup>+</sup> , adenosine 5'-triphosphate (ATP), serotonin (5-HT), acetylcholine, cytokines and growth factors released from damaged tissues; histamine may yield an itching sensation
Thermal/mechanical nociceptors	Strong mechanical stimulus combined with temperature >45°C or <10°C, activating heat/mechanical or cold/mechanical nociceptors
Polymodal nociceptors	Strong mechanical, thermal (>45°C or <10°C), chemical stimuli in combination of two types of stimulus or more

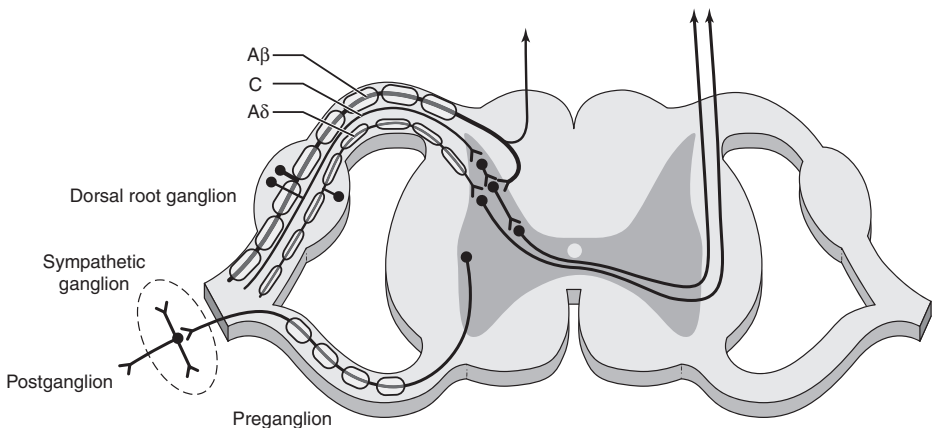
activated resulting in slight increase of pain sensations but also in an increased activity in endogenous pain inhibiting systems.

### Itch

It has been postulated that pruritus receptors (Schmelz et al., 1997; Liu et al., 2009) are part of a larger set of nociceptors where activation of the whole group elicits pain while activation of the itch-selective subset elicits exclusively itch. However, itch or pruritus is not just triggered in the peripheral tissue but also more centrally suggesting that there exist multiple neural pathways for itch induction (Misery et al., 2014).

## ACUPUNCTURE AND MECHANORECEPTORS

Acupuncture may activate all types of mechanoreceptor in superficial-cutaneous and in deep muscular tissue (Figs. 3.1 and 3.2). It has been reported that most acupuncture points contain abundant free nerve endings, encapsulated cutaneous receptors (Merkel, Meissner, Ruffini and Pacinian corpuscles), sarcous sensory receptors (muscle spindles and tendon organs) as well as ergo-receptors, and their afferent fibres. Acupuncture sites can be classified into three types: muscle-spindle-rich acupuncture sites, cutaneous-receptor-rich acupuncture sites and tendon-organ-rich acupuncture sites. In acupuncture practice manipulation is often performed on the inserted needles to enhance needling sensation and therapeutic responses. Different modes of stimulation technique used (e.g. superficial versus deep needling depth, light or no stimulation versus rotation and thrusting) will probably determine which type of receptor is activated. Gentle and repetitive manipulation of the inserted needle would be expected to produce mechanical pressure and tissue distortion that activate mechanoreceptors. Also, manual stimulation may result in distant effects which has been attributed to shear force- and stress-induced tissue displacements. All types of manual technique tested have yielded greater distant effects on sarcous stretch receptors than cutaneous mechanoreceptors; twist/rotation has the greatest distant effects on the cutaneous superficial and deep receptors as well as sarcous stretch receptors compared to other techniques. In addition, the sensitivity status of the peripheral terminals, i.e. intact or sensitised as in a pain condition, will be influenced by the receptor's peripheral milieu such as the presence of lactate,  $K^+$ ,



**Figure 3.2** Components of an afferent nerve and the possible sites of interaction between its constituent different nerve fibre types. There are two distinct functional categories of axon primary afferents with cell bodies in the dorsal root ganglion, and sympathetic postganglionic fibres with cell bodies in the sympathetic ganglion. Primary afferents include those with large-diameter myelinated ( $A\alpha, \beta$ ), small-diameter myelinated ( $A\delta$ ) and unmyelinated (C) axons. All sympathetic postganglionic fibres are unmyelinated.

nitric oxide (NO) ions, chemokines, cytokines, myokines and a number of other factors. Therefore, the same stimulation technique may produce very different sensations ranging from being barely detectable to being painful.

## RECEPTIVE FIELDS

The peripheral region from which a sensory receptor and thereby the neuron is excited is called its receptive field. The size and structure of receptive fields differ for receptors in the superficial and deep tissue layers. A single DRG neuron innervating superficial tissue layers receives input from a cluster of Merkel disc receptors or Meissner's corpuscles. In contrast, each nerve fibre innervating deeper layers of skin receives input from a single Ruffini ending or Pacinian corpuscle, i.e. these receptors cover large areas of skin with indistinct borders. Commonly, these receptive fields have a single 'punctum maximum' where the sensitivity to touch is greatest and which is located directly overlying the receptor.

## ADAPTATION

Mechanoreceptors differ in adaptation properties and are overall classified into being slowly and rapidly adapting. The slowly adapting receptors like the Merkel disc receptors and the Ruffini endings signal the pressure and shape of objects by their average firing rates (the duration of the stimulus). Rapidly adapting receptors like the Meissner's corpuscle and the Pacinian corpuscle register motion of objects. These receptors respond during the period when the position of a stimulus changes and stop firing when it comes to rest. These rapidly adapting receptors also register vertical impact (vibration) and lateral motion (stroking, rubbing or palpation).

## SENSORY THRESHOLD

Mechanoreceptors also differ in sensory threshold, i.e. the minimum intensity of stimulation required to generate an action potential. Rapidly adapting receptors have lower thresholds than slowly adapting receptors. The Pacinian receptors are the most sensitive mechanoreceptor and sense the frictional displacement of the skin. Whereas the Meissner's corpuscles detect and localise small bumps since they are sensitive to abrupt changes in the shape of objects, more prominent bumps and/or edges are required to activate the slowly adapting Merkel disc receptor. The strongest response occurs when a punctate probe, like an acupuncture needle, or a sharp edge contacts the receptive field. This could explain why a punctate probe feels relatively sharp as opposed to a blunt sensation of a cotton bud.

## AFFERENT NERVE FIBRES

All somatosensory information from the limbs and trunk is transmitted through individual peripheral afferent nerve fibres of spinal DRG neurons, each of which responds to the modality-specific type of stimulation associated with the morphological and molecular specialisation of its peripheral receptors (Kandel et al., 2013). Somatosensory information from cranial structures is transmitted by the trigeminal sensory neurons in the brain stem, which are functionally and morphologically homologous to spinal DRG neurons, and transmitted further to higher levels in the brain via second order neurons. The principal functions of dorsal ganglion neurons and the trigeminal nerve are transduction of the stimulus and transmission of encoded stimulus information to the higher levels of the central nervous system (CNS). Starting at the DRG level there is an interaction, a 'cross talk', between different stimulation modalities (Table 3.3).

**TABLE 3.3 ■ Overview of activity in peripheral receptors and their nerve fibres in response to different stimulation modalities**

Type of receptor/tissue	Type of nerve fibre	Stimulation modality/sensation
<i>Mechanoreceptor/superficial-cutaneous, deep-subcutaneous</i>		<i>Touch</i>
Meissner's corpuscle	A $\alpha$ , $\beta$	Stroking
Merkel disc receptor	A $\alpha$ , $\beta$	Pressure
Pacinian corpuscle	A $\alpha$ , $\beta$	Vibration
Ruffini ending	A $\alpha$ , $\beta$	Skin stretch
Hair	A $\alpha$ , $\beta$ , $\delta$	Stroking
Cutaneous touch, CT	C	Stroking
<i>Mechanoreceptors/joint, tendon, muscle</i>		<i>Proprioception/movement</i>
Muscle spindle, primary	A $\alpha$ /type Ia	Muscle stretch (length)
Muscle spindle, secondary	A $\beta$ /type II	Muscle stretch
Ergo-receptor (pressure sensitive)	A $\delta$ /type III	Muscle contraction
Golgi tendon organ	A $\alpha$ /type Ib	Muscle contraction
Joint capsule	A $\beta$ /type II	Joint angle
Stretch-sensitive free endings	A $\delta$ /type III	Stretch-passive, active force
<i>Thermal receptors/superficial-cutaneous, deep-subcutaneous, joint/tendon/muscle</i>		<i>Temperature</i>
Cool receptors	A $\delta$ /type III	Temp. 18–35°C/coolness
Warmth receptors	C/type IV	Temp. 30–45°C/warmth
<i>Nociceptors, uni-/polymodal/superficial-cutaneous, deep-subcutaneous, joint, tendon, muscle</i>		<i>Nociception, itch/pain, itch</i>
Cold nociceptors	C/type IV	Temp. <10°C/cold
Heat nociceptors	A $\delta$ /type III	Temp. >45°C/heat
Mechanical	A $\delta$ /type III	Strong mechanical stimulation/sharp pricking pain
Heat–mechanical	A $\delta$ /type III	Temp. >45°C, strong mechanical stimulation/burning pain
Cold–mechanical	C/type IV	Temp. <10°C, strong mechanical stimulation/freezing pain
Chemical	C/type IV	Release of chemical compounds
Polymodal	C/type IV	Temp. >45°C, <10°C; strong mechanical stimulation, release of chemical compounds/deep burning pain

Recent studies also indicate that somatosensory stimulation may be transmitted to the nucleus tractus solitarius without bypassing the DRG.

Mechanoreceptors and proprioceptors are commonly innervated by large-diameter myelinated afferents axons, whereas thermal receptors and nociceptors have small myelinated or unmyelinated axons. Large fibres, A $\alpha$ /I fibres, conduct action potentials at 70–120 m s<sup>-1</sup>, medium sized A $\beta$ /II at 35–70 m s<sup>-1</sup> and small myelinated A $\delta$ /III at 5–35 m s<sup>-1</sup>. The unmyelinated afferent nerve fibres conduct action potentials at 0.2–2.0 m s<sup>-1</sup>. This difference in conduction velocity may be attributed to internal resistance to current flow along the axon including the saltatory conduction activity due to the spacing of the nodes of Ranvier. Gentle, dynamic touch is encoded by a distinct

tactile type receptor, C Tactile (CT) afferents, and transmitted in unmyelinated afferent nerves found exclusively in hairy skin. CT afferents increase firing when the skin is stroked at a speed of  $\sim 30 \text{ mm s}^{-1}$  with gentle contact at a typical skin temperature (Olausson et al., 2002; Löken et al., 2009; Morrison et al., 2010; Ackerley et al., 2014).

The presence of somatic afferent and efferent fibres innervating skin, connective tissues, and skeletal muscles has been reported at acupuncture points. Many of the acupuncture sites investigated had relatively dense neural components, particularly nerves fibres, with a ratio of nearly 1.4:1 compared to nonacupuncture points. Also, the ratio of myelinated to unmyelinated fibres was found to be nearly fourfold higher in the acupuncture point Zu-San-Li (ST36) than surrounding areas. Sarcous sensory receptors (muscle spindles and tendon organs) and their afferent fibres have been reported to be concentrated at acupuncture points located on thick muscles such as the tibialis anterior and rectus femoris muscles (Li et al., 2004).

Another important neural component of most acupuncture sites, and indeed many somatic areas, is the dense and fine autonomic nerve fibres, found in close proximity to the sensory receptors and afferents. Most autonomic nerves are norepinephrine (NE) containing sympathetic fibres but also cholinergic acetylcholine (ACh) parasympathetic efferent nerves may be found. Interaction between somatic and autonomic neural components may serve to modulate local and afferent signals in points where acupuncture stimulation is applied.

Interaction between activity in the sensory afferents and autonomic efferent nerve fibres may also take place in the DRGs and at segmental level in the spinal cord as well as in more central parts of the CNS (see Figure 3.2).

## ELECTRICAL STIMULATION OF AFFERENT NERVES

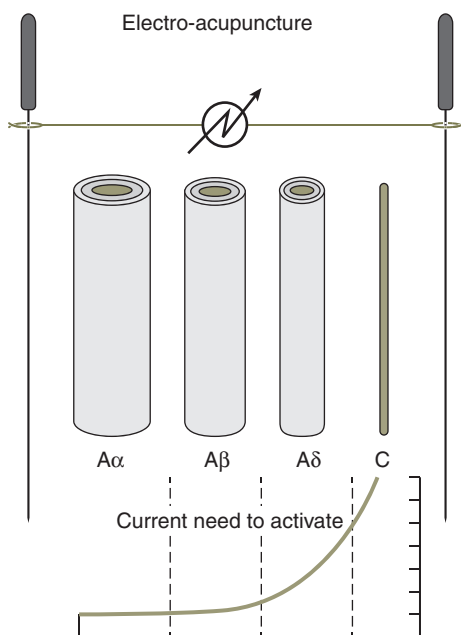
As stated earlier, the difference in the conduction velocities of different nerves may be attributed to internal resistance to current flow along the axon. This is also the reason why electrical nerve stimulation using either surface electrodes as in transcutaneous electrical nerve stimulation (TENS), or with thin needles connected to an electrical stimulator as in electro-acupuncture (EA), with low intensity, activates afferent nerves with large diameter more easily than the thinner ones (Barlas and Lundberg, 2006). When using higher stimulation intensities, thinner sensory afferents are activated by the stimulus (Figure 3.3).

Due to the fact that EA results in the electrical activation of many different afferent nerves, it is therefore not to be regarded as equivalent to manual acupuncture (Napadow et al., 2005). It is generally accepted that manual acupuncture sets up activity in superficial and deep A $\beta$  and A $\delta$  fibres but that most of the clinical effects including pain alleviation and autonomic modulation may be attributed to the activation of deep A $\beta$ , A $\delta$  and C fibres (Andersson and Lundberg, 1995).

## Peripheral substrate of the *de qi* sensation

A large body of empirical and experimental evidence suggest that during acupuncture stimulation the so called needling sensation, *de qi*, should be strived for (Figure 3.4).

Although the perception of needling sensation may vary between individuals and with manual techniques, this distinct sensation is generally characterised by soreness, numbness, heaviness, distension and aching in the deep tissues surrounding the inserted needle (Hui et al., 2010). The *de qi* sensation is also often accompanied by an increased blood flow and a feeling of warmth at the acupuncture point. Simultaneously with the patients' sensation of *de qi*, the acupuncturist often perceives an increased resistance to further movement/manipulation of the inserted needle. Thus, the needling sensation is not a single, but a compound sensation that is generated from the activation

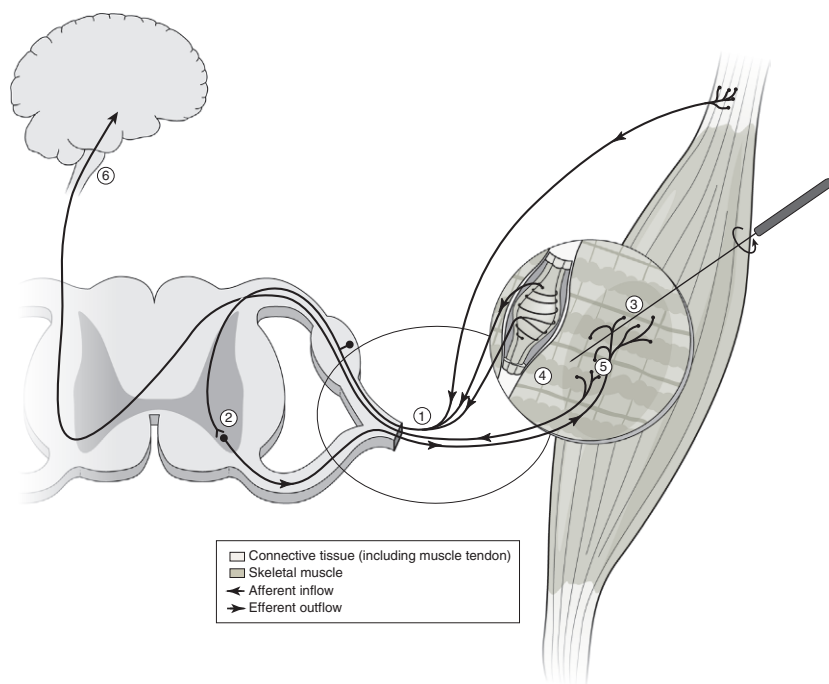


**Figure 3.3** Schematic illustration of the relationship between fibre diameter and stimulation intensity (current/voltage) needed for their activation.

of various sensory receptors and their afferent fibres in acupuncture sites. It has been demonstrated that numbness, heaviness and distension during needling are closely associated with the activation of myelinated A $\beta$  and A $\delta$  afferents in deep tissues of acupuncture points, whereas aching and soreness are associated with stimulation of small myelinated A $\delta$  and unmyelinated C fibres.

## LOCAL HYPER OR HYPOESTHESIA FOLLOWING ACUPUNCTURE

The insertion of acupuncture needles into various tissues has been reported to result in the release of mediators that can be classified as inhibitory or stimulatory. The stimulatory mediators include various cytokines, prostaglandins (PGs), bradykinin and other pro-inflammatory factors that enhance afferent fibre excitability at the acupuncture site. The inhibitory mediators include ACh, NE, gamma amino butyric acid (GABA),  $\beta$ -endorphin, SP, somatostatin, NO, adenosine 5'-triphosphate (ATP), cyclic guanosine monophosphate and adenosine, which suppress receptor and/or afferent fibre excitability at the acupuncture site. The predominant effect of acupuncture is to enhance the release of inhibitory mediators. Serotonin (5-HT) and histamine are also released but the effect is more complex as they can exert either inhibitory or stimulatory effects, depending upon which receptors they act on. The increase of mediators in local, peripheral tissues is partly originating from non-neuronal cells. Local mechanisms at acupuncture sites may play an important role in acupuncture-induced analgesia, in which afferent noxious signals from sites distal to needling points are blocked mostly by enhancing the activity of inhibitory mediators and activating negative feedback in acupuncture sites based on autoreceptors to SP and CGRP (Zhang et al., 2012).



**Figure 3.4** A schematic presentation of the scenario behind the *de qi* sensation evoked from skeletal muscle. Sequence of events: **(1)** The acupuncture needle penetrates skin, connective tissue surrounding the muscle and the muscle. **(2)** When the needle is gently twirled the dynamic fibres of the muscle spindle are activated sending signalling of ‘shortening of the muscle’ in  $A\alpha, \beta$  fibres to the spinal cord. **(3)** A reflex is evoked at the spinal cord level resulting in the activation of  $A\alpha$  motor neurons. **(4)** Activity in the  $A\alpha$  motor neurons results in the contraction of the muscle surrounding the needle which is perceived as local resistance. **(5)** Further stimulation of needle (twirling and thrusting) results in the activation of local ergo-receptors conducting their information in  $A\delta$  fibres to the spinal cord that there is a strong local muscle contraction. Also, from the ergo-receptors there is a release of CGRP (see text). **(6)** The afferent activity set up at the spinal cord level is further transmitted to the brain and perceived as numbness, heaviness and distension or *de qi*.

## Segmental innervation – dermatomes, myotomes and sclerotomes

The area of skin that is innervated by a single spinal nerve is termed a dermatome and the corresponding innervation areas for muscle and skeletal tissue are termed myotome and sclerotome (see [Appendix 1](#)). In fact, the boundaries of the dermatomes, myotomes and sclerotomes are less distinct than commonly shown on distribution maps because the axons making up a spinal nerve originate from different peripheral nerves. Similarly, separate peripheral nerves contribute axons to several adjacent spinal nerves, leading to overlap in the area innervated by each segment in the spinal cord.

## Spinal cord/trigeminal nucleus/brain

Central axons of DRG neurons branch at their entry into the spinal and trigeminal nucleus and project to nuclei in the spinal cord grey matter and brainstem. The spinal grey matter is divided into three functionally distinct regions: the dorsal horn (laminae I–VI), the intermediate zone

(laminae VII) and the ventral horn (laminae VIII–IX). Lamina X consists of grey matter surrounding the central canal. The sensory specialisation of DRG neurons is maintained in the CNS through distinct ascending pathways. The modalities such as nociception, hard pressure, cutaneous touch and temperature are relayed through synapses in the spinal cord/trigeminal nucleus to the contralateral anterolateral quadrant, where axons ascend to the brain stem and thalamus in the anterolateral system. Nerve impulses induced by touch and proprioception are transmitted directly to their nucleus in the medulla through ipsilateral dorsal columns, the dorsal column-medial lemniscal system, before being transmitted to the thalamus and higher brain centres.

## CROSS TALK AT SPINAL CORD LEVELS

The spinal cord's dorsal horn in the CNS is a key region in which sensory information is received, integrated and relayed to higher brain structures. The patterns of termination of primary afferents within the spinal cord are related to axonal diameter, receptive field and sensory modality. Nociceptive primary afferents terminate primarily in the superficial part of the dorsal horn, specifically in laminae I and II, whereas inputs from myelinated A $\beta$  fibres of mechanoreceptors terminate in deeper layers, i.e. laminae III/IV. Thus, touch sensitive fibres terminate deeper and nociceptive sensitive fibres terminate more superficially within the dorsal horn. Excitatory and inhibitory interneurons are found throughout laminae I, II and III/IV. Neurons in lamina V receive convergent excitatory input from both non-nociceptive A $\beta$  fibres and nociceptive A $\delta$  and C fibres, conveying the 'strongest' stimulation to the higher centres of the CNS. Furthermore, the large diameter A $\beta$  fibres inhibit the firing frequency of neurons in lamina V by activating inhibitory interneurons in laminae I/III. On the other hand the A $\delta$  and C fibres excite lamina V neurons but also inhibit the firing of the inhibitory interneurons in lamina II, which are activated by the A $\beta$  fibres.

In a study using intersectional genetic manipulations to identify some critical components of mechanical pain transduction, it was reported that peripheral mechanical nociceptors and A $\beta$  mechanoreceptors, together with spinal somatisation excitatory and dynorphin inhibitory neurons, form a microcircuit that transmits and gates mechanical pain (Duan et al., 2014).

In summary, non-nociceptive afferents close and nociceptive afferents open a 'gate' to the central transmission of noxious input. Approximately 30% of the neurons in the superficial dorsal horn are immune-reactive for the inhibitory transmitter GABA, and/or glycine. These inhibitory neurons are driven by the activity in low-threshold primary A $\beta$  afferents. However, it has recently been demonstrated that nearly all of the GABA containing neurons also receive input from high-threshold A $\delta$  and/or C fibres, a combination that is not predicted by the gate control theory of pain. On the other hand, glycine containing inhibitory neurons located near the laminae II/III border may directly inhibit an enzyme that is a member of protein kinase family and involved in diverse cellular signalling pathways, the protein kinase C  $\gamma^+$  neurons, to close the gate. Some lamina II neurons receive tonic descending inhibition from higher brain areas via GABA and glycine containing neurons, suggesting that superficial dorsal horn neurons are inhibited through two different modes, phasic and tonic, that could be activated through peripheral and central mechanisms. Depending on the pain condition treated, possibly the short term effects of acupuncture are mediated through the phasic activity whereas the long-term effects are related to modulation of the tonic activity. This gate mechanism described earlier is the rationale for the use of TENS for the relief of pain (Barlas and Lundberg, 2006).

The mechanism of analgesia is topographically specific, meaning that the area of the body in which pain is regulated is linked anatomically to the segments where the nociceptive and non-nociceptive afferents terminate. This would suggest that the sensory stimulation should be applied in the same segments (dermatome, myotome or sclerotome) as the pain. Furthermore, activity in non-nociceptive afferents results in inhibition of sympathetic efferents in lamina VII of the

spinal cord, whereas nociceptive activity results in an activation (e.g. during needling). However, long-term needling (20–40 min) may result in the activation of centrally based inhibition of the sympathetic tone. This inhibition is more pronounced after the end of treatment and may last for hours. An even more potent counterbalance to nociception is mediated by stimulation of the periaqueductal grey (PAG) region, the grey matter that surrounds the third ventricle and the central aqueduct. This stimulation-produced analgesia activates descending pain inhibitory systems that inhibit firing of nociceptive neurons in the dorsal horn of the spinal cord. Few neurons in the PAG matter project directly to the dorsal horn of the spinal cord. Instead, they make excitatory connections with neurons, in particular serotonergic neurons, in the nucleus of raphe magnus. From the neurons in nucleus raphe magnus they project to the spinal cord via the dorsal part of the lateral funiculus and make inhibitory connections with neurons in laminae I, II and V of the dorsal horn. Other descending inhibitory systems that suppress the activity of the nociceptive neurons in the spinal cord originate in the noradrenergic locus coeruleus and block the output of the neurons in laminae I and V by direct and indirect inhibitory actions. They also interact with opioid-containing circuits in the dorsal horn. Opiates and opioid peptides (endorphins, enkephalins and dynorphins) regulate nociceptive transmission via different mechanisms – one of these is postsynaptic inhibition, produced by increasing  $K^+$  conductance in the second order neuron, and one is presynaptic inhibition. The opioid-induced decrease in transmitter release (glutamate and SP) from primary afferents results either indirectly from a decrease in  $Ca^{2+}$  entry into the sensory terminals or directly from a decrease in  $Ca^{2+}$  conductance.

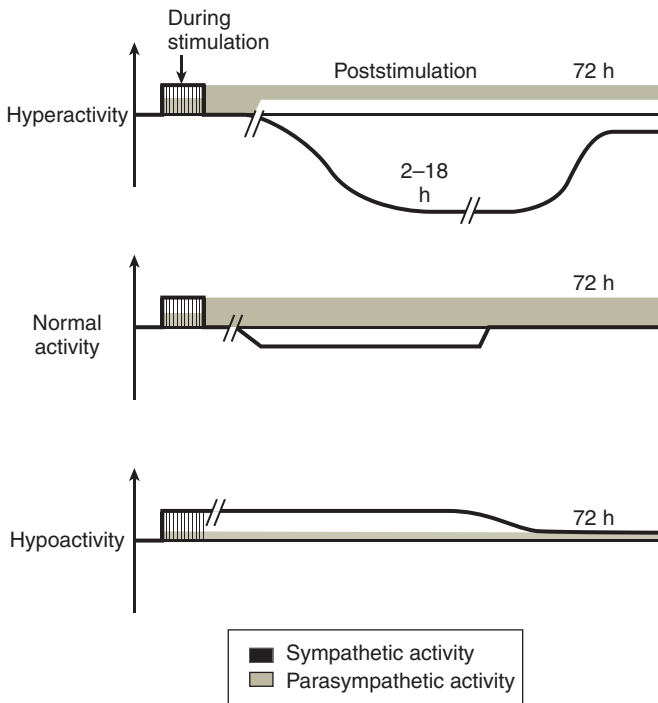
Both experimental and clinical studies suggest that part of the analgesic effect of acupuncture is mediated through activity in these descending systems that also seem to play a role in the modulation of the autonomic activity. A role for opioids is supported by the fact that morphine produces analgesia by activating descending inhibitory systems.

## SPINAL REFLEXES – DORSAL ROOT, MOTOR AND AUTONOMIC REFLEXES

It has been demonstrated that descending inhibitory systems modulate dorsal root reflexes (DRR) through presynaptic inhibition and thereby inhibition of the antidromic activity in A and C primary afferent nerve fibres that contributes to the release of SP and CGRP at their peripheral terminals, so called neurogenic inflammation. This descending control of DRR is seen following activation of neurons in PAG and is mediated by GABA and 5-HT. GABA (A) receptors play a key role in the generation of DRRs, but 5-HT<sub>(3)</sub> receptors also contribute.

The spinal cord processes somatic and visceral reflexes as well as outputs from the CNS to effector organs involved in visceral functioning including cardiovascular regulation. Since opioid or nociceptin-like immuno-reactivity is present in the spinal sympathetic nuclei (i.e. intermediolateral column, IML) it has been suggested that acupuncture, especially low frequency (2 Hz) EA, also influences the neurotransmission between the brain stem and the IML. Interestingly, both opioids and nociceptin reduce the response to rostral ventrolateral medulla-induced sympathetic excitation, indicating that the two peptides can regulate sympathetic outflow. Furthermore, afferent stimulation can modulate sympathetic activity directly through the inhibition of excitatory interneurons. These interneurons appear to form important links in the spinal cord circuitry involved in autonomic control. Taken together this suggests that acupuncture, via modulation of somato-autonomic reflexes, may modulate for example gut motility and bladder activity, a modulation that is directly related to the physiological/pathophysiological state of the organ/system (Cortelli et al., 2013).

As shown in Figure 3.5, there is an increased sympathetic activity during acupuncture stimulation (manual or electro). After the end of stimulation the effects are dependent on the basal activity before the start of stimulation. In subjects with an increased activity before the start of



**Figure 3.5** Modulation of sympathetic tone. Schematic illustration of the effects of acupuncture on sympathetic and parasympathetic activity during and after stimulation.

stimulation there is a sympathetic inhibition that may last as long as 12 h. In patients with a normal tone there is a minor inhibition which is short-lasting. In subjects with a low activity the activity stays increased after the end of stimulation. The parasympathetic tone is also affected but with a lesser magnitude but possibly with a longer duration (up to 72 h). The total net effect is a response towards the 'normal level'.

It has also been demonstrated that acupuncture may modulate motor reflexes at the spinal cord level as well as motor behaviour, a modulation dependent on the condition treated. For example, manual acupuncture provides sufficient neuromuscular stimuli to promote immediate changes in motor unit gross recruitment without repercussion in maximal force output in healthy subjects, whereas poststroke patients did not exhibit significant reduction on the myoelectric activity and maximal force output after manual acupuncture. A common clinical experience is that acupuncture reduces muscle tenderness. This has in part been attributed to the suppression in motor neuronal activities of the skeletal muscles by needle insertion. In a healthy human, application of vibratory stimulation on the volar side of the fingertip induces a flexion reflex. Typically, the finger flexion force occurs with the onset of vibration and increases progressively during vibration. This reflex is assumed to have two reflex arcs, that is, the spinal short loop and supraspinal long loop. Interestingly, the activities in both these loops are suppressed by ipsilateral segmental acupuncture stimulation in the upper extremity, and suppression on the supraspinal long loop is relatively long lasting (a continuous decrease of the vibration-induced finger flexion reflex was observed after removal of a needle) compared with that on the short loop. This motor reflex inhibiting effect has been attributed to the activation of nociceptive A delta or C fibres indicating that there is convergence between nociceptive and non-nociceptive afferents of different origins onto the common interneurons in segmental reflex pathways to  $\alpha$ -motor neurons. This would suggest that noxious

somatosensory input by using acupuncture could suppress motor neurons that innervate the flexor muscles through common interneurons and that acupuncture treatment could be a useful intervention for reducing muscle spasticity at least in the upper extremity (Takakura et al., 2010). The effect of acupuncture on motor reflexes and motor control needs further evaluation.

## SPINAL GLIAL CELLS

Spinal astrocytes have emerged as important contributors to findings of hyper-phenomena in pathological and chronic pain such as hyperalgesia and allodynia. Experimental studies have shown that acupuncture stimulation inhibits the activity in spinal astrocytes and nociceptive reactions in inflammation and that this inhibition is associated with the activation of spinal  $\alpha_2$  adrenoceptors.

## THE DORSAL COLUMN-MEDIAL LEMNISCAL SYSTEM

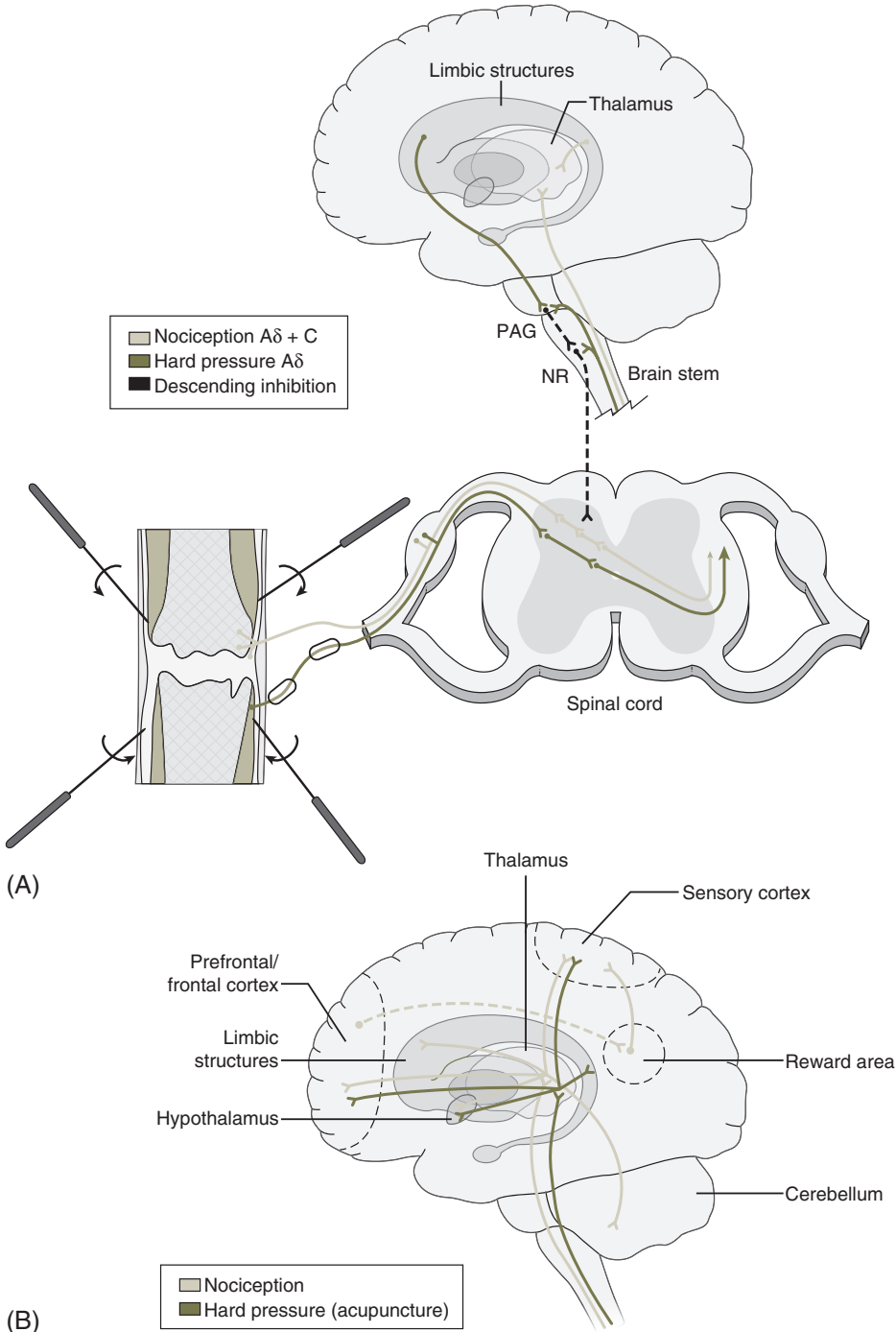
The principal central branch of the axon of neurons mediating tactile sensation and proprioception from the limbs and trunk ascends in the spinal cord in the ipsilateral dorsal column to the medulla (Kandel et al., 2013). At the upper spinal levels the dorsal column is divided into two fascicles (bundles) – the gracile fascicle and the cuneate fascicle. The medially located gracile fascicle contains fibres that ascend from the ipsilateral sacral, lumbar and lower thoracic segments. The cuneate fascicle is located laterally and contains fibres from the upper thoracic and cervical segments. Axons from the two bundles terminate in the lower medulla, in the gracile nucleus and the cuneate nucleus, respectively. The axons from the two nuclei cross to the other side of the brain stem and ascend to the posterior lateral nucleus of the thalamus. Mechanosensory information from the face and scalp is transmitted to the principal trigeminal nucleus which is located in the pons.

The trigeminal lemniscus crosses over and later joins axons from the arm and back of the head in the medial lemniscus. Because of the crossing of fibres in the medulla and pons the right side of the brain receives sensory input from the limbs and trunk of the left side of the body and vice versa. From the thalamus the proprioceptive sensory input projects, directly and indirectly, to the somatosensory cortex, the frontal cortex, the limbic structures and the hypothalamus.

## THE ANTEROLATERAL SYSTEM

Neurons mediating information of nociception/pain, hard pressure, cutaneous touch and temperature from the limbs and trunk terminate in the ipsilateral dorsal horn of the spinal cord. The fibres are small and branch extensively in the white matter, forming the tract of Lissauer, and terminate in the most superficial layers of the dorsal horn. Thus neurons in the marginal zone (lamina I) and substantia gelatinosa (laminae II and III) respond almost exclusively to painful or thermal stimulus. From the dorsal horn the information ascends to the anterolateral quadrant of the contralateral side of the spinal cord (Figure 3.6). The anterolateral pathway is thus made up by neurons in the marginal zone, the nucleus proprius (lamina IV), the deep layers of the dorsal horn (laminae V and VI) and the intermediate zone (lamina VII). The anterolateral tract includes three ascending pathways, terminating in the thalamus: the spinothalamic pathway, the spinoreticular pathway and the spinomesencephalic pathway. The spinothalamic pathway mediates information about the nociceptive/painful and thermal stimuli directly to the ventral posterior lateral nucleus of the thalamus. Axons in the spinoreticular tract will synapse with neurons in the reticular formation of the medulla and pons, which then relay information to the intralaminar and posterior nuclei of the thalamus and to other structures in the diencephalons, such as the hypothalamus.

Trigeminal sensory afferents that carry information of nociception/pain and temperature from the head and face form the spinal trigeminal tract, terminating in the trigeminal nucleus in the medulla. The spinal trigeminal nucleus contains a marginal zone and a substantia gelatinosa that



**Figure 3.6** (A) Brainstem mechanisms. Schematic illustration of the activation of descending inhibition. (B) Central mechanisms. Schematic illustration of the central mechanisms of acupuncture.

receive nociceptive information and a magnocellular division that is innervated by mechanoreceptors and corresponds to the nucleus proprius. The axons of trigeminal neurons also decussate in the brain stem and join ascending fibres from the most rostral spinal segments.

Thalamic neurons sensitive to nociceptive/painful or thermal stimuli project to the primary somatic sensory cortex, to the dorsal anterior insular cortex and to the anterior cingulate gyrus. In addition to these regions, activity is conveyed to the frontal cortex, the limbic structures and the hypothalamus.

## BRAIN

Studies using fMRI for evaluation of treatment effects have demonstrated that acupuncture can induce haemodynamic changes in brain functional networks. Although brain responses vary slightly in response to stimulation of different acupuncture points, similar central effects are generally obtained when acupuncture stimulation is associated with sensations of *de qi*. Under these circumstances acupuncture stimulation evokes deactivation of a limbic–paralimbic–neocortical network, which encompasses the limbic system, as well as activation of somatosensory brain regions. Also, extensive signal attenuations, mainly distributed in the medial temporal lobe, the posterior cingulate cortex, the medial prefrontal cortex and a large section of the parietal cortex has also been reported. These networks closely match the default mode network (DMN) and the anti-correlated task-positive network (Hui et al., 2010). The amygdala and hypothalamus, in particular, show decreased activation during acupuncture stimulation that is not commonly associated with DMN activity. On the other hand when sharp uncomfortable pain is elicited there is no deactivation and instead activation and arousal may be seen.

The default network, the dominant functional network during the resting state, plays an important role in attention, memory, consciousness and self-referential processes. During illness, pain and stress, the network's activity is disturbed resulting in malfunctioning. When subjected to acupuncture the default mode has been reported reset and patients may report the 'return of their mental functioning'. Similarly, acupuncture, but not the sham version, can also induce the increased connectivity within both the DMN and the sensorimotor network.

Acupuncture can also cause prominent and long-lasting modulation effects on the intrinsic coherence of the wide interceptive-autonomic areas of the brain and spinal cord. Acupuncture may furthermore inhibit activity in the frontal cortex, thereby modulating anxiety responses and fear avoidance reactions. Recently, behavioural and functional brain responses to the insertion of needles into the body have been recorded in two different contexts, treatment and stimulation. Although the applied stimuli were physically identical in both groups, the verbal instructions differed: participants in the stimulation group were primed to consider the acupuncture as a painful stimulus, whereas the participants in the treatment group were told that the acupuncture was part of therapeutic treatment. Acupuncture yielded greater brain activation in reward-related brain areas (ventral striatum) of the brain in the treatment group when compared to the stimulation group. Also, brain activation in response to pain stimuli was significantly attenuated in the bilateral secondary somatosensory cortex and the right dorsolateral prefrontal cortex in the treatment group but not in the stimulation group demonstrating the power of context in acupuncture practise (Lee et al., 2014).

## Clinical points

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Taken together, the peripheral effects of acupuncture on the sensory nerves may be attributed to changes in the peripheral milieu of the sensory receptors and their afferents, reflex mechanisms at the spinal cord level, activation of descending modulation as well as deactivation of the limbic–paralimbic–neocortical network. Also, acupuncture may result in deactivation of the frontal–prefrontal areas of the brain as well as modulation of hypothalamic homeostatic mediated responses.

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## Neuro-immunological reflex components

### AXON REFLEX

In addition to orthodromic inputs to the spinal cord and brain from the periphery, action potentials in sensory neurons can also be transmitted antidromically at branch points back down to the periphery, thereby forming the axon reflex. These activities together with sustained local depolarizations lead to a rapid and local release of neural mediators from both peripheral axons and terminals.

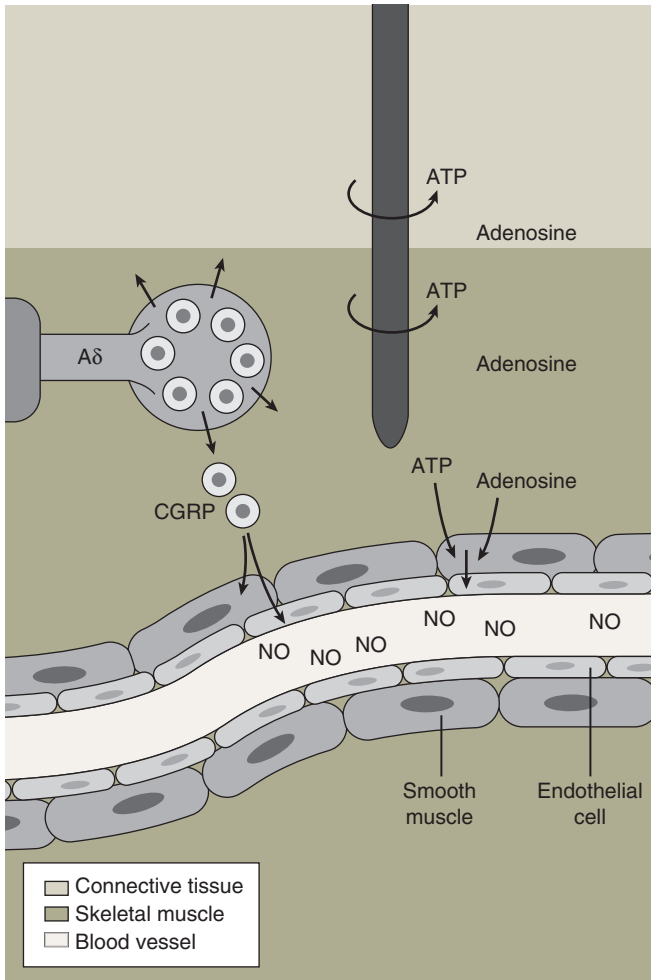
### AXON REFLEX – A $\delta$ /TYPE III FIBRES

Intense antidromic stimulation of afferent nerves sufficient to excite thin myelinated A $\delta$ /type III fibres will produce an increase in skin and muscle blood flow in the distal territory of the nerve, as shown in [Figure 3.7](#). The magnitude and time course of the vasodilatation depend on the number and frequency of the nerve stimulations. There is no evidence of an accompanying plasma extravasation, suggesting that A $\delta$ /type III afferent nerve fibres are involved in axon reflex/axon ([Jansen et al., 1989](#); [Shinbara et al., 2013](#)) response reactions without inducing a neurogenic inflammation (this includes the activation of C afferent fibres, see in the succeeding text). This could explain part of the positive effects of acupuncture when treating ischemic conditions, i.e. acupuncture stimulates ergo-receptors and so releases CGRP and triggers A $\delta$ /III axon reflexes that in turn results in vasodilation and increased capillary flow mainly within the muscle. Two pathways for the vasodilation of CGRP have been described, either NO-endothelium dependent or not:

1. CGRP binds to the CGRP1 receptor on vascular smooth muscle cells and induces an increase in intracellular cyclic adenosine 5'-monophosphate (cAMP) and protein kinase A. This cascade results in opening of K<sup>+</sup> ion channels and Ca<sup>2+</sup> ion sequestration followed by relaxation of vascular smooth muscle (vasodilation). This pathway is NO-endothelium-independent.
2. The binding of CGRP to the CGRP1 receptor on vascular endothelium cells triggers NO production via NO synthase. NO released from vascular endothelium leads to relaxation of vascular smooth muscle. This pathway is NO-endothelium-dependent.

A peripheral role for CGRP in the vasodilatory response following acupuncture is also partly supported by studies showing that CGRP participated in increasing local muscle blood flow following manual acupuncture ([Shinbara et al., 2013](#)) without changing arterial blood pressure in intact rats. Other mechanisms involved in the vasodilatory response such as release of adenosine phosphate compounds from connective tissue or by an increase in mechanical signalling through the extracellular matrix were also suggested. These compounds may induce its vasodilatory effect by binding to adenosine (A1 receptors) and purine receptors (P2Y receptors). The binding of adenosine phosphate compounds to their receptors on vascular endothelium cells induces in turn release of NO. The release of NO could also be the result of a sequential reaction, beginning with a change in sympathetic activity and leading to NO production. Another explanation could be that NO production may be caused by mechanical stimulation of the vascular endothelium, i.e. shear stress imposed on the vascular wall, during acupuncture ([Langevin et al., 2013](#)).

The earlier results suggest that acupuncture may have an important role in the peripheral tissue milieu by inducing vasodilation. NO is possibly the most important factor in the short term (reversing ischaemia), whereas CGRP may be more important in the longer term as it has trophic effects on the endothelium, thereby promoting angiogenesis. The relevance of this mechanism needs to be elucidated in pathophysiological models and in clinical conditions.

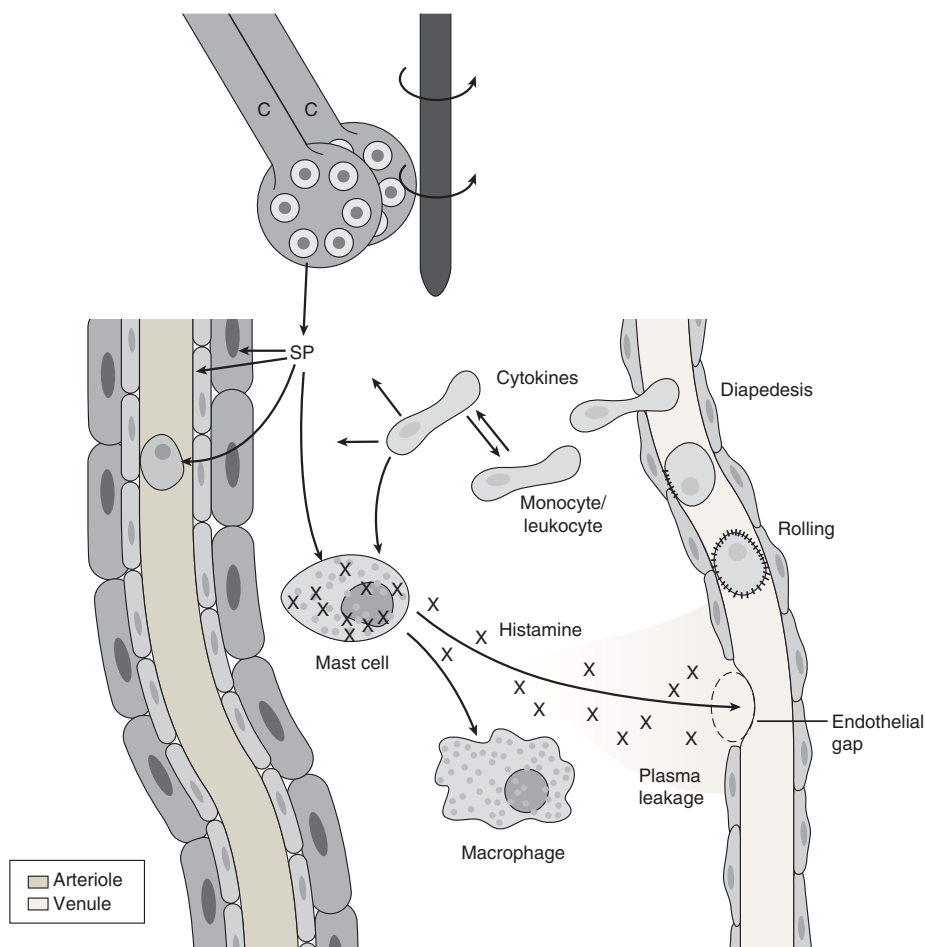


**Figure 3.7** Axon reflex. The antidromic action potentials in ergo-receptor afferent branches stimulate the release of CGRP from the ergo-receptors. A, adenosine; ATP, adenosine 5'-triphosphate; CGRP, calcitonin gene related peptide; NO, nitrous oxide.

## AXON REFLEX – C/TYPE IV FIBRES

Acupuncture may also result in the activation of nociceptors and C fibres (Tjen-A-Looi et al., 2005). Action potentials transmitted in nociceptor neurons result in a rapid and local release of neural mediators from both peripheral axons and terminals inducing vasodilation, extravasation and oedema, i.e. 'neurogenic inflammation' (Fig. 3.8), an inflammatory response independent of that produced by the immune system. In the acute setting of tissue damage, it has been suggested that neurogenic inflammation is protective, facilitating physiological tissue healing.

Neurogenic inflammation is mediated by the release of CGRP and SP, which act directly on vascular endothelial and smooth muscle cells. CGRP has potent vasodilatory effects as described earlier, whereas SP increases capillary permeability leading to plasma extravasation and oedema.



**Figure 3.8** Neurogenic inflammation induced by the axon reflex. The antidromic action potentials in nociceptor afferent branches stimulate the release of SP from peripheral terminals. Here, DRG, dorsal root ganglion; 5-HT, serotonin; PGs, prostaglandins; and BK, bradykinin.

Also mediators such as glutamate, NO and cytokines are released from the peripheral sensory neurons that in turn will directly attract and activate innate (mast cells, dendritic cells) and adaptive immune cells (T lymphocytes).

Cytokines have a key role in communication between immune cells and nociceptor neurons. Upon activation of cytokine receptors, signal transduction pathways are activated in sensory neurons leading to downstream phosphorylation of membrane proteins including tryptophan and voltage-gated channels. The resulting sensitization of nociceptors means that normally innocuous mechanical and heat stimuli can now activate nociceptors. Interleukin (IL) 1 beta and tumour necrosis factor (TNF) -alpha are two important cytokines released by innate immune cells during inflammation that are directly sensed by nociceptors which in turn express the cognate receptors and induce activation of p38 map kinases, leading to increased receptor membrane excitability. Nerve growth factor (NGF) and PG E2 are also major inflammatory mediators released from immune cells that act directly on peripheral sensory neurons to cause sensitization. An important

effect of nociceptor sensitization caused by immune factors is an increased release of neuropeptides at peripheral terminals that further activate immune cells, thereby inducing a positive feedback loop that drives and facilitates hypersensitivity.

In the early phases of inflammation, sensory neurons signal to tissue resident mast cells and dendritic cells, which are innate immune cells that are important in initiating the immune response. During the effector phase of inflammation, immune cells need to find their way to the specific site of injury. Many mediators released from sensory neurons, neuropeptides, chemokines and glutamate, are chemotactic for neutrophils, eosinophils, macrophages and T cells, and enhance endothelial adhesion which facilitates immune cell homing. Furthermore, neurons may directly participate in the effector phase of the inflammatory reaction, as neuropeptides themselves may have direct antimicrobial functions. Neuronally derived signalling molecules can also direct the type of inflammation, by contributing to the differentiation or specification of different types of adaptive immune T cells. An antigen is phagocytised and processed by innate immune cells, which then migrate to the nearest lymph node and present the antigenic peptide to naïve T cells. Depending on the type of antigen, co-stimulatory molecules on the innate immune cell, and the combinations of specific cytokines, naïve T cells mature into specific subtypes that best serve the inflammatory effort to clear the pathogenic stimulus. This T cell maturation process is heavily influenced by sensory neuronal mediators.

Considering that signalling molecules released from peripheral sensory nerve fibres regulate not only small blood vessels, but also the chemotaxis, homing, maturation and activation of immune cells, it is becoming clear that neuro-immune interactions are very intricate. Furthermore, it is specific combinations of signalling molecules released from nociceptors that influence different stages and types of immune responses rather than individual neural mediators. This would suggest that the effects of acupuncture are different depending on when, where and how it is applied. Clinical observations have demonstrated that the acupuncture-induced axon reflex is strongly apparent in the areas of acupuncture points, particularly in the back and abdominal acupuncture points. It is characterised by a hyperaemia (flare) that rapidly (generally within 2–5 min) spreads beyond needling points of the skin with a diameter of 1–3 cm (see [Fig. 34.1](#)). The axon-dorsal root reflex at acupuncture sites may also be closely related to dense sympathetic nerve-rich arterioles.

Hypothetically the local neurogenic inflammation induced by acupuncture may play an important role in tissue healing, such as in tendinopathies. This would further suggest that needling in the proper site (injured site) is critical for these specific effects.

## AUTONOMIC REFLEXES

Acupuncture and EA may result in the activation of interneurons in the brainstem including the nucleus tractus solitarius that results in outgoing neural signals from the dorsolateral motor nucleus. The outgoing signals generated in the brainstem suppress innate immune responses and inflammation, either: via the vagus nerve to the adrenal medulla (vagal-adrenal medulla reflex), resulting in the release of dopamine; or via the adrenergic nerve to the blood vessel near the fifth lumbar segment (exercise gateway reflex); or via the vagus nerve to the coeliac ganglion to the spleen to acetylcholine-producing (AChT+) T cells (inflammatory reflex); or they induce a local axon reflex (see in the preceding text). Also, there is neural influence on B cell trafficking and antibody secretion affecting the immune response. Furthermore, outgoing signals are also relayed to the nuclei in the hypothalamus that control the function of the hypothalamo-pituitary-adrenal (HPA) axis, resulting in increased glucocorticoid hormone release by the adrenal gland, which suppresses innate immune responses.

## VAGAL-ADRENAL MEDULLA REFLEX

The efferent vagus nerve signals induce the release of dopamine in the adrenal medulla resulting in the activation of dopaminergic type 1 (D1) receptors and suppressed systemic inflammation. The route by which sensory signals elicited from EA transit to the brainstem to activate outgoing vagus signals remains unknown. Interestingly, there is a significant correlation between depressed vagus nerve activity and increased morbidity and mortality in non-resolving inflammatory diseases. An intriguing possibility is that vagus nerve deficiencies might be reversed by vagus nerve stimulation using for example EA, aerobic exercise, meditation, music therapy and biofeedback training.

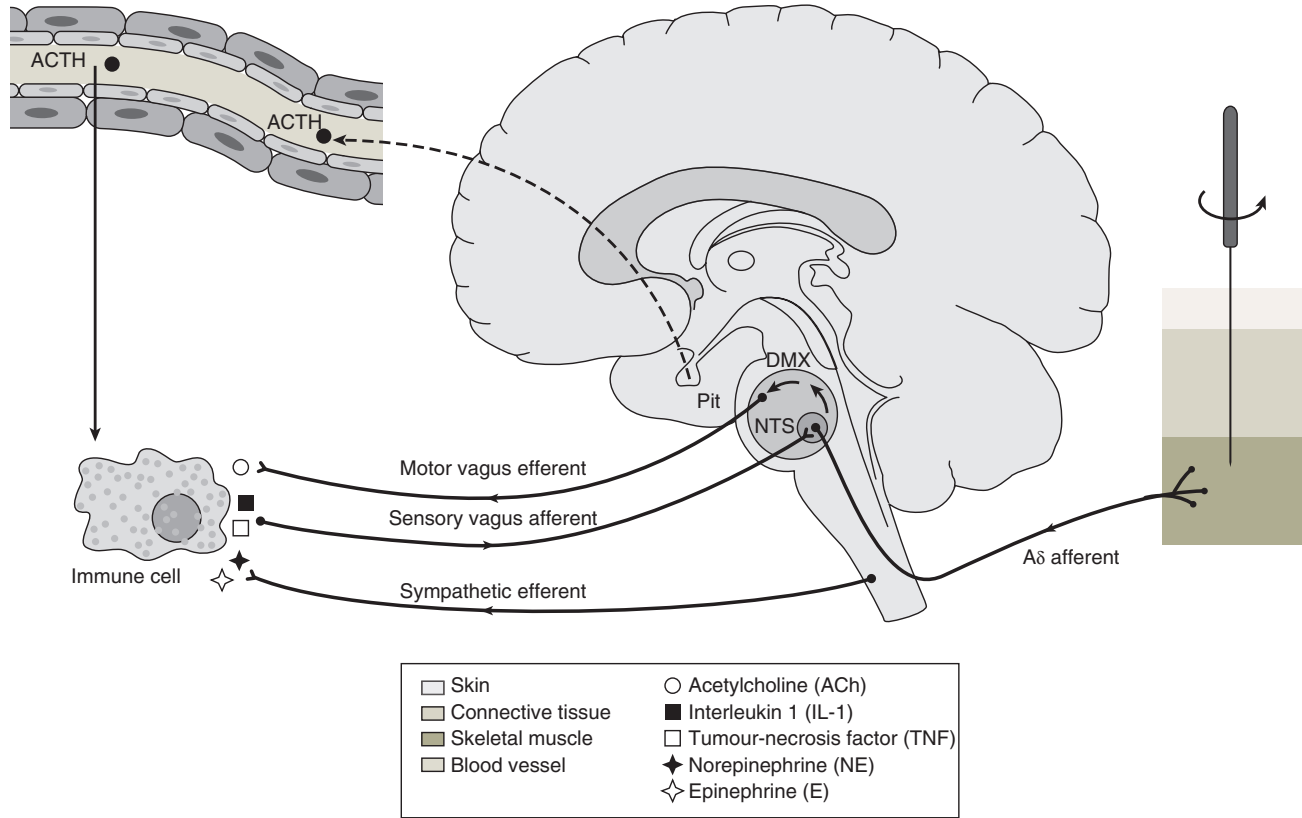
## INFLAMMATORY REFLEX

In the inflammatory reflex ([Fig. 3.9](#)), products of inflammation activate afferent action potentials travelling in the vagus nerve to the nucleus tractus solitarius, which relays the neuronal signals to other brain nuclei located in the hypothalamus and brainstem ([Watkins et al., 1995, 1999](#); [Goehler et al., 1997](#)). Efferent signals travel from the nucleus ambiguus and dorsal motor nucleus back down the vagus nerve, which terminates in the coeliac ganglia ([Berthoud and Powley, 1996](#); [Borovikova et al., 2000b](#)). Stimulation of the vagus nerve activates adrenergic splenic neurons residing in the coeliac ganglion, which travel into the spleen and terminate in synapse-like structures adjacent to T cells in the white pulp ([Rosas-Ballina et al., 2009](#)). NE released from splenic neurons binds to  $\alpha_2$  adrenergic receptor expressed on a subset of T cells that expresses choline acetyltransferase, the rate-limiting enzyme in acetylcholine biosynthesis.

Activation of the sympathetic outflow by flight-or-fight responses or pain, or through direct signalling, can increase local concentrations of adrenaline and noradrenaline, which can suppress inflammation further. Anatomical, functional and molecular lesions in the vagus nerve enhance cytokine production associated with non-resolving inflammation ([Tracey, 2007](#)). Under basal conditions, the vagus nerve transmits tonic inhibitory activity that dampens the activity of the innate immune response to pathogen associated molecular products ([Rosas-Ballina et al., 2009](#)). The inhibitory activity of the inflammatory reflex can be enhanced by manual acupuncture or EA that increase the generation of adrenergic signals in the splenic nerve ([Borovikova et al., 2000a,b](#); [Bernik et al., 2002](#); [Metz and Tracey, 2005](#); [Tracey, 2002](#); [Vida et al., 2011](#)). The activity of the splenic adrenergic neurons can be functionally modified by either preganglionic neurons arising in the sympathetic chain, or by signals arriving there from the vagus nerve that terminate on interneurons residing in the coeliac ganglion that can modulate the signals arising from the sympathetic chain. Activation of the sensory sciatic nerve by EA in the leg inhibits cytokine release and improves survival in an experimental model of sepsis through a sciatic-to-vagus nerve circuit that regulates the innate immune response ([Torres-Rosas et al., 2014](#)). Signals in the sciatic nerve results in efferent vagal nerve activity and dopamine release in the adrenal medulla (see in the preceding text).

## EXERCISE GATEWAY REFLEX

The muscle contraction dependent reflex or the ‘exercise gateway reflex’ circuit that regulates T cell recruitment into the CNS ([Arima et al., 2012](#)) has several components. In this reflex circuit, sensory signals arise in the hind limb, are transmitted to the spinal cord and brain stem and then descend in the sympathetic chain to be relayed via adrenergic neurons that terminate on endothelial cells to regulate expression of chemokine receptors ([Tracey, 2012](#)). A similar circuit, termed the ‘exercise pressor reflex’, is activated during exercise by stimulation of mechanoreceptors and metabolically sensitive ergo-receptors in skeletal muscle ([Kaufman and Hayes, 2002](#)). Arrival at the brain stem level of sensory input from muscles increases the activity of cholinergic neurons



**Figure 3.9** Inflammatory products produced in damaged tissues activate afferent signals that are relayed to the nucleus tractus solitarius; subsequent activation of vagus efferent activity inhibits cytokine synthesis through the cholinergic anti-inflammatory pathway (the inflammatory reflex). Information can also be relayed to the hypothalamus and the dorsal vagal complex to stimulate the release of ACTH, thereby activating the humoral anti-inflammatory pathway. Activation of the sympathetic outflow by flight-or-fight responses or pain, or through direct signalling, can increase local concentrations of adrenaline and noradrenaline, which can suppress inflammation further. Pit, pituitary; DMX, dorsolateral motor nucleus; NTS, nucleus tractus solitarius; ACTH, adrenocorticotrophic hormone.

descending in the sympathetic chain at the same segmental level, i.e. it has a somatotopic organisation. This suggests that EA via sensory sciatic nerve stimulation may initiate anti-inflammatory efferent vagus nerve signals (Chavan and Tracey, 2014).

## NEURAL INFLUENCE ON B CELL TRAFFICKING AND ANTIBODY SECRETION

Electrical stimulation of the vagus nerve may influence B cell trafficking and antibody secretion. Stimulation of the vagus nerve results in the activation of the adrenergic splenic nerve. This leads to accumulation of CD11+ B cells in the marginal zone of the spleen and decreased antibody production. On the other hand, in the setting of diminished signalling from the vagus nerve to splenic nerve, antibody-secreting CD11+ B cells traverse the marginal zone and enter the red pulp of the spleen, where they release antibodies into the circulation (Mina-Osorio et al., 2012). The net effect of this neural regulation is that the antibody levels to specific antigenic challenge is significantly reduced thereby influencing the adaptive immune response.

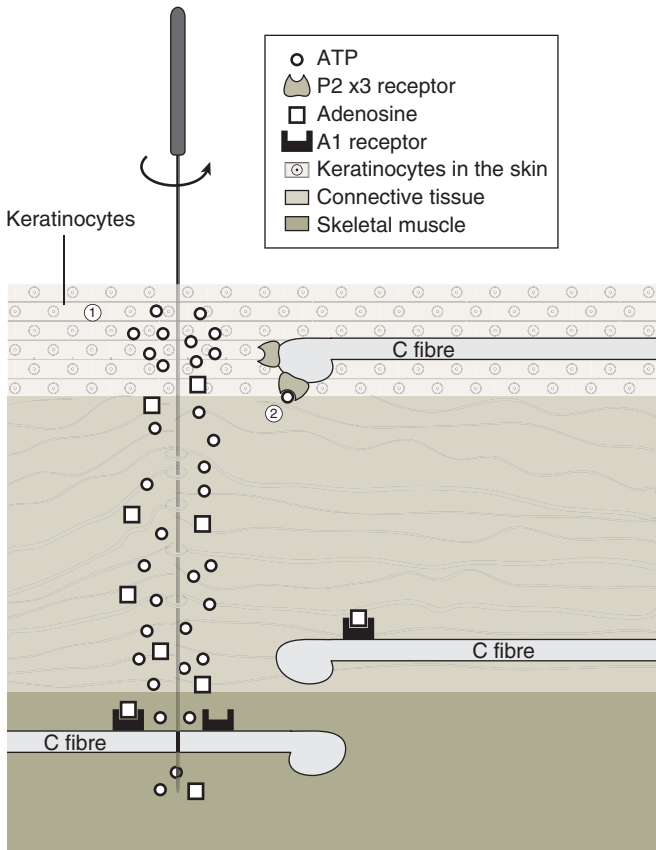
## Connective tissue

Acupuncture stimulation has been reported to induce mechanical deformation in connective tissue resulting in mechanical stimulation of fibroblasts resulting in autocrine purinergic signalling, active changes in fibroblast cell shape, anisotropic tissue motion and a small tissue lesion (Fig. 3.10).

## AUTOCRINE PURINERGIC SIGNALLING

Acupuncture, as well as other modes of mechanical stimulation of fibroblast and other cell types, is associated with the release of purines like ATP (Burnstock and Verkhratsky, 2009) that is present within the cytosol of all cell types (Sawynok, 2011). The mechanical stimulation may result in opening of mechanosensitive channels of the plasma membrane and thus in release of cytosolic ATP (Goldman et al., 2010; Takano et al., 2012).

Recently, it was found that acupuncture on mouse ST36 significantly reduced chronic pain in the ipsilateral paw and increased the extracellular concentrations of ATP and adenosine in acupuncture point tissues. ATP is well established as an intracellular energy source that powers biochemical processes but is also proposed to act as an extracellular signalling molecule between cells. The specific receptors on the cell surfaces that receive messages carried by ATP are termed purinoceptors since ATP belongs to the purine group. It is been reported that ATP can be released from different types of cell (e.g. osteoblasts, fibroblasts, endothelial, epithelial and glial cells) in response to gentle mechanical stimulation without damaging the cells. ATP is also released in response to heat and electrical stimulation techniques in conjunction with acupuncture to enhance its effect. Recent evidence has also confirmed the finding that sensory nerve terminals in the skin are activated by ATP or inhibited by adenosine. Interestingly, the local application of 2-chloro-N(6)-cyclopentyladenosine, an adenosine A1 receptor agonist, replicated the analgesic effect of acupuncture. The local inhibition of enzymes involved in adenosine degradation also potentiated the acupuncture-elicited increase in adenosine, as well as its anti-nociceptive effect. These data strongly suggest that acupuncture-released ATP and its metabolite adenosine in local acupuncture point tissues block nociceptive impulses from sites distal to needling point (Goldman et al., 2010; Zylka, 2010). Also, adenosine binds to endothelial cells resulting in the release of NO and thereby a marked vasodilation. ATP is thereby increased in extracellular fluid as it leaks out when the plasma membrane is damaged during the mild tissue injury associated with acupuncture.



**Figure 3.10** Insertion and twisting of the needles employed in acupuncture mechanically deforms the skin, leading to the release of ATP by skin keratinocytes (1). ATP binds to specific receptors located on sensory nerve endings in the skin known as P2X3 and P2X2/3 (2). The signalling message is then relayed via dorsal root ganglia to the spinal cord and subsequently through inter-neuronal pathways to the brain stem which contains motor neurons that control the functions of gut, lung, heart, arteries and reproductive organs, all major targets for acupuncture. Signals also travel to pain centres in the cortex, delivering a message to inhibit pain.

Alternatively, or in addition, ATP can be actively released by local cells (Burnstock and Verkhratsky, 2009). Samples collected near the location of the needle have shown that the concentrations of all purines are increased in tissue close to the stimulated area (Takano et al., 2012). Potent enzymes, ectonucleotidases, present in the interstitial space degrade ATP to adenosine 5'-diphosphate, adenosine 5'-monophosphate (AMP) and adenosine, each of which has their own respective sets of receptors (Zimmermann, 2000). In particular the adenosine A1 receptor has been shown to suppress the conductance of nociceptive input by activating A1 receptors on peripheral pain fibres (Lynch et al., 2003; Inoue et al., 2004; Zylka, 2010). In support of a key role of A1 receptors in the peripheral mechanisms by which acupuncture may reduce pain is the observation that A1 receptor knockout mice do not benefit from acupuncture or from local injection of adenosine A1 receptor agonists (Goldman et al., 2010).

## CHANGES IN FIBROBLAST CELL SHAPE

A series of studies have demonstrated that connective tissue is affected by acupuncture. For example it has been shown that rotation of an inserted acupuncture needle stretches nearby connective tissue by pulling collagen fibres from the periphery toward the needle (Langevin et al., 2001). Also, acupuncture needle rotation cause fibroblasts to increase their cross-sectional area, as their cell bodies expand and spread out (Langevin et al., 2005, 2006a,b, 2007). Tissue stretching is associated with a transient increase in tissue tension, but the viscoelastic properties of the tissue return to prestretching level within minutes, which occurs in parallel with active remodelling of the cytoskeleton of fibroblasts (Langevin et al., 2011). Tissue tension is likely sensed by fibroblasts by their adhesion to collagen fibres (Tomasek et al., 2002). Interestingly, pretreatment with rho kinase inhibitors (Zhou and Petroll, 2010) or colchicine (inhibitor of microtubule polymerization) is linked to a 60–80% greater resting tissue tension after tissue stretching and prevents the expansion of fibroblasts (Langevin et al., 2011). These observations suggest that the remodelling of fibroblasts in response to mechanical stimulation dampens the increase in tissue tension induced by tissue stretch and thereby is important for maintaining stable viscoelastic properties of the tissue (Abbott et al., 2013). Thus, the cytoskeleton of fibroblasts plays an important role in dynamic tissue remodelling.

Fibroblasts located close to the location of needle stimulation are not only exposed to the changes in tissue tension induced by needle rotations, but also to ATP. Recent findings suggest that activation of purinergic receptors will in turn trigger a transient disassembly of polymerized actin, an effect that may contribute to the rapid cytoskeletal remodelling and cell body expansion induced by tissue stretch. It has therefore been suggested that acupuncture-induced purine signalling (da Rocha Lapa et al., 2012; Nakav et al., 2008) triggers fibroblast cytoskeletal remodelling that counteracts fibrosis such as in scar tissue, and that purinergic signalling via increases in cytosolic  $\text{Ca}^{2+}$  may contribute to such dynamic changes of the actin cytoskeleton (Goldman et al., 2013).

## ANISOTROPIC TISSUE MOTION

It has previously been shown using ultrasound elastography in humans that acupuncture needle manipulation causes measurable movement of tissue up to several centimetres away from the needle. Rotation of the needle following insertion promotes the mechanical coupling between the needle and connective tissue, and causes winding of tissue surrounding the needle. This mechanical signal (passive deformation) is transmitted to connective tissue cells and is amplified due to increased tissue displacement. The superficial area of tissue deformation may reach 25 mm<sup>2</sup> or more around a single needle and stimulates several muscle and tendon receptors, evidenced by the variety of subjective descriptions (of aching, pressure, heaviness or soreness) of the *de qi* sensation. Also, it has been shown that fibroblasts within whole areolar connective tissue expand and develop larger cross-sectional areas in response to acupuncture (Langevin et al., 2006a, 2007). Recently, anisotropic tissue motion was observed during acupuncture, a motion that may influence the spatial distribution of local connective tissue cellular responses following acupuncture needle manipulation (Fox et al., 2014). This response suggests that different directions of rotation of an acupuncture needle may have different effects at the same site.

It is well known that manual acupuncture and EA may produce local and distant effects (see in the succeeding text). EA stimulation produces the distant effects in exciting cutaneous mechanoreceptors and sarcous stretch receptors at acupuncture sites, with a range of ~25–45 mm from needling point. The EA intensity-dependent distant effect was observed on only the cutaneous superficial receptors, but not the cutaneous deep receptors and sarcous stretch receptors in rabbits (Andersson and Lundeberg, 1995). In general, while most nociceptors are

innervated by thin myelinated A $\delta$  and C fibres, most somatic mechanoreceptors are innervated by A $\beta$  fibres. Therefore, the activation of mechanoreceptors and their A $\beta$  afferent fibres appears to play a dominant role in the biophysical reactions of acupuncture sites, particularly in muscle-spindle-rich acupuncture sites.

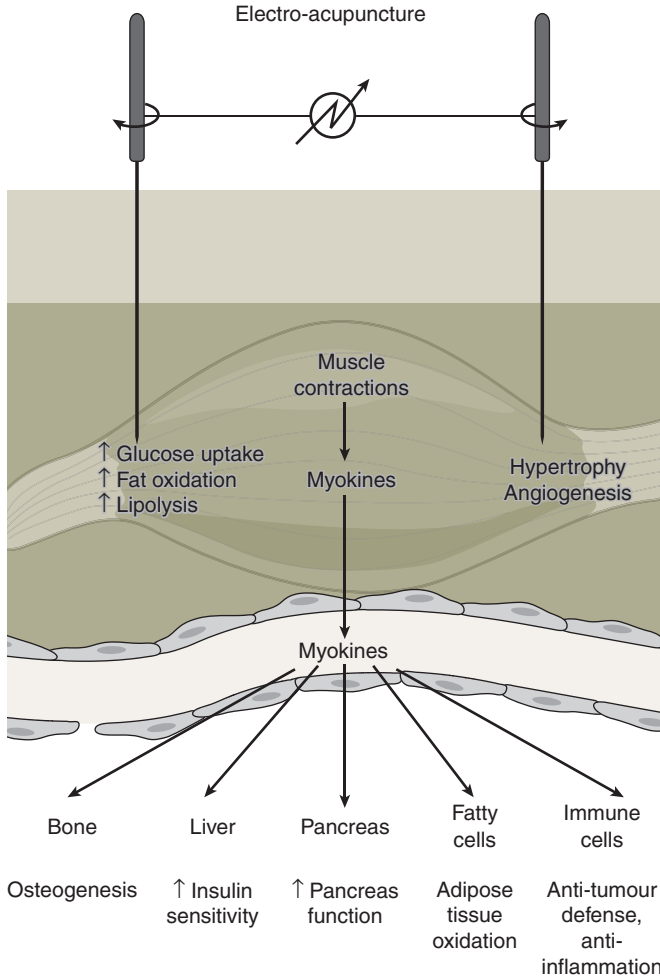
## Skeletal muscle

Skeletal muscle is the largest organ in the body and primarily associated with locomotion. Also, recent evidence suggest that skeletal muscle acts as a secretory organ through the release of 'myokines', i.e. cytokines and other peptides that are produced, expressed and released by skeletal muscle especially during contractions (Pedersen et al., 2007). This provides a basis for how acupuncture, through the activation of skeletal muscle, may communicate with the stimulated muscle and with other organs in the peripheral parts of the body (Figure 3.11).

During the past decade, skeletal muscle cells have been identified as cells that have the capacity to produce several hundred transmitters, myokines, including: ILs, growth factors, and modulatory factors including hormones. Several of these myokines are released during both manual and EA (Lundeberg, 2014). Furthermore, the efficacy of acupuncture has been attributed to the elicitation of strong muscle contractions and the effects on organ functions by acupuncture are similar to those obtained by protracted exercise (Andersson and Lundeberg, 1995). Preliminary trials suggest that part of the beneficial effects of repeated low frequency EA stimulation of muscle tissue also may be attributed to significant alterations in DNA methylation (in gene bodies and intergenic regions) and gene expression. The direction of the changes of DNA methylation was inversely correlated to expression changes which is concordant with phenotypic adaptations, i.e. the muscle adapts to being active. This would suggest that EA, low frequency TENS or other types of electrical muscle stimulation may be used to reduce the consequences of inactivity as seen following postsurgical immobilisation.

## INTERLEUKINS

IL-6 is released into the blood stream in response to muscle contractions and possibly low frequency EA (Pedersen and Febbraio, 2008). Following exercise, the basal plasma IL-6 concentration may increase up to 100-fold, but smaller increases of ~10-fold are seen following EA. The exercise-induced increase of plasma IL-6 occurs in an exponential manner and the peak IL-6 level is reached at the end of the exercise or shortly thereafter (Fischer et al., 2004; Ostrowski et al., 1998; Pedersen, 2000; Rosendal et al., 2005). The amount of IL-6 produced is correlated to the amount of muscle mass engaged in the exercise. Interestingly, the concentration of IL-6 within the contracting skeletal muscle is 5- to 100-fold higher than the levels found in the circulation (Bergfors et al., 2005; Hirose et al., 2004; Nosaka and Clarkson, 1996). Also, it has been shown that IL-6 appears to accumulate within the contracting muscle fibres as well as in the interstitium during exercise (Jonsdottir et al., 2000). Muscle-derived IL-6 appears to function as an exercise sensor (Hoene and Weigert, 2008; Pedersen, 2012; Ruderman et al., 2006). Thus, enhanced glucose availability and training adaptation attenuate the exercise-sensitive increase in IL-6 plasma concentration (Fischer et al., 2004). Contraction may lead to IL-6 gene transcription via Ca<sup>2+</sup> being released from the sarcoplasmic reticulum to activate IL-6 through activation of nuclear factor of activated T cells (Holmes et al., 2004). A role of IL-6 in the local glucose metabolism is supported by the finding that a trained muscle is more sensitive to IL-6 and that insulin-resistant individuals show IL-6 resistance (Scheele et al., 2012). This could explain why elevation of circulating levels of IL-6 has been reported to accompany obesity and physical inactivity, i.e. serving as a compensatory mechanism. This suggestion is in line with studies showing that IL-6 enhances glucose production and uptake and cytokine signalling through AMP-activated protein



**Figure 3.11** Myokines released within the muscle and into the blood stream during acupuncture stimulation of skeletal muscle fibres. LIF, IL-4, IL-6, IL-7 and IL-15 promote muscle hypertrophy. Myostatin inhibits muscle hypertrophy and exercise leads to the release of a myostatin inhibitor, follistatin, from the liver. BDNF and IL-6 are involved in AMPK-mediated fat oxidation and IL-6 enhances insulin-stimulated glucose uptake and stimulates glucose output from the liver, but only during exercise. IL-6 stimulates lipolysis and IL-15 stimulates lipolysis of visceral fat. IL-6 also enhances insulin-stimulated glucose uptake; IL-6 also increases insulin secretion by inducing the expression of GLP-1 by the L cells of the intestine. IL-6 has anti-inflammatory effects as it inhibits TNF production and stimulates the production of IL-1ra and IL-10. Furthermore, IL-6 stimulates cortisol production and thereby neutrocytosis and lymphopenia. IL-8 and CXCL1 might be angiogenic. IGF-1, FGF-2 and TGF- $\beta$  are involved in bone formation, and follistatin-related protein 1 improves endothelial function and revascularization of ischaemic blood vessels. Irisin and meteorin-like have a role in 'browning' of white adipose tissue. IGF-1 and FGF-2 are involved in bone formation, and follistatin-related protein 1 improves endothelial function and revascularization of ischemic vessels. Irisin has a role in 'browning' of white adipose tissue. Abbreviations: AMPK, 5'-AMP-activated protein kinase; BDNF, brain-derived neurotrophic factor; FGF-2, fibroblast growth factor 2; FGF-21, fibroblast growth factor 21; FSTL-1, follistatin-related protein 1; GLP-1, glucagon-like peptide 1; IGF-1, insulin-like growth factor-1; IL, interleukin; IL-1ra, IL-1 receptor antagonist; LIF, leukaemia inhibitory factor; TGF- $\beta$ , transforming growth factor  $\beta$ . (Reproduced from Pedersen, B.K., 2013. Muscle as a secretory organ. *Compr. Physiol.* 3, 1337–1362.)

kinase (AMPK) (Pedersen and Febbraio, 2012). It appears that IL-6 activates AMPK in skeletal muscle by increasing the concentration of cAMP, and secondarily, the AMP: ATP ratio (Kelly et al., 2009). It has also been reported that IL-6 stimulates lipolysis in skeletal muscle (Petersen et al., 2005) and has a role in myogenesis and mediates anti-inflammatory effects (Pedersen, 2013).

IL-7 is a cytokine that is required for T and B cell development. It has also been shown to be a myokine that may act on satellite cells and may be involved in myogenesis (Haugen et al., 2010).

IL-8 is a chemokine that increases in contracting muscles in response to exhaustive exercise such as running, which involves eccentric muscle contractions (Nieman et al., 2001, 2002, 2003; Suzuki et al., 2003). IL-8 possesses neutrophil chemo-attractant activity and is also involved in the processes of angiogenesis through the activation of microvascular endothelial cells via the CXC (family of chemokines) receptor 1 and 2, CXCR1 and CXCR2 (Kim et al., 2010; Li et al., 2003).

IL-15 is a cytokine that belongs to the IL-2 superfamily and was originally isolated on the basis of its ability to support natural killer T-lymphocyte proliferation. IL-15 is expressed in a variety of non-lymphoid tissues, and has been identified as an anabolic factor that is highly expressed in skeletal muscle (Grabstein et al., 1994). Furthermore, IL-15 has been suggested to play a role in muscle-adipose tissue interaction (Argiles et al., 2005) with high expressions in skeletal muscle and placenta. IL-15 has been identified as having anabolic function in muscle growth (Furmanczyk and Quinn, 2003). IL-15 seems also to play a role in reducing adipose tissue mass, as IL-15 decreases lipid deposition in preadipocytes and decreases the mass of white adipose tissue (Carbo et al., 2001. Booth et al., 2012).

## GROWTH FACTORS

Neurotrophins are a family of structurally related growth factors, including NGF and brain-derived neurotrophic factor (BDNF), which exert many of their effects on neurons primarily through Trk receptor tyrosine kinases. BDNF and its receptor TrkB are expressed in the brain as well as in skeletal muscle following EA and exercise (Huang and Reichardt, 2001; Pedersen et al., 2009; Pedersen, 2011). Possibly this could account for the therapeutic effect of acupuncture and exercise in neurodegenerative diseases (Matthews et al., 2009). In the muscle, BDNF increased phosphorylation of AMPK and acetyl-CoA carboxylase and enhanced fat oxidation (Pedersen et al., 2009; Pedersen, 2011). This suggests that BDNF released from skeletal muscles plays a role in the peripheral metabolism, myogenesis and muscle regeneration (Sakuma and Yamaguchi, 2011). Fibroblast growth factor-2 (FGF-2) is an insulin-regulated myokine, which induces hepatic expression of PGC-1 $\alpha$ , a key transcriptional regulator of energy homeostasis (Domouzuglou and Maratos-Flier, 2011). Moreover, FGF-2 causes corresponding increases in fatty acid oxidation, tricarboxylic acid cycle flux and gluconeogenesis. It has also been suggested that FGF-2 may play a role in muscle – bone interaction by repair and healing of injured and diseased tendons. Insulin-like growth factor-1 is a myokine that is up-regulated in skeletal muscle downstream of Akt signalling and in regenerating muscle in response to injury (Pedersen, 2012).

## TGF- $\beta$ SUPERFAMILY

Myostatin is a member of the transforming growth factor beta (TGF- $\beta$ ) superfamily that is produced by skeletal muscle and secreted into the circulation (Rodgers and Garikipati, 2008). It inhibits muscle growth and is also involved in the modulation of adipose tissue function and mass (Allen et al., 2008; Feldman et al., 2006; Guo et al., 2009; Lin et al., 2002). Both aerobic exercise and resistance training in humans and animals attenuate myostatin (Allen et al., 2011). Follistatin, another member of the TGF- $\beta$  superfamily, is a naturally occurring inhibitor of myostatin that

is released from the liver during acute exercise and EA (Walsh, 2009). Also, follistatin-like 1 (FSTL-1) activates Akt-endothelial nitric oxide synthase (eNOS) signalling in endothelial cells and appears to have cardio-protective effects (Shimano et al., 2011). Over-expression of FSTL-1 stimulates ischemia-induced revascularization in mice through activation of eNOS.

## IRISIN

Irisin is released into the circulation by muscle activity during exercise (Boström et al., 2012) and possibly EA. Irisin drives the transformation of white fat cells into bright cells, i.e. white fat cells with a phenotype similar to that of brown fat cells (Wu et al., 2012). This is demonstrated by a marked increase in the expression of uncoupling protein 1 in white adipose tissue. An elevated level of plasma irisin is followed by a reduction in body weight and an improvement in metabolic homeostasis (Lin et al., 2005; Wenz et al., 2009) suggesting that it may be used as a marker of the effect of acupuncture in obesity.

## LEUKAEMIA INHIBITORY FACTOR

Leukaemia inhibitory factor (LIF) is a myokine that acts as a stimulus for platelet formation, proliferation of hematopoietic cells, bone cell formation, neural cell survival and formation, muscle satellite cell proliferation and acute phase production by hepatocytes (Hilton et al., 1988). LIF is normally expressed at a low level in type 1 muscle fibres but is augmented in mechanically overloaded muscle and in denervated rat muscle suggesting that endogenous LIF production is modulated by factors influencing muscle activity (Kami and Senba, 1998; Spangenburg and Booth, 2006). Furthermore, LIF restores the hypertrophic response to increased loading (Spangenburg and Booth, 2006). Another function of LIF is the potency to induce myoblast proliferation and inhibit differentiation of myoblasts into multinucleated myotubes (Spangenburg and Booth, 2002; Diamant and Tushuizen, 2006; Sun et al., 2007).

## ERYTHROPOIETIN

Erythropoietin (EPO) is a kidney-produced hormone with distinct effects on erythropoiesis that is also produced by skeletal muscle and thus also classified as a myokine (Hojman et al., 2009). In skeletal muscle locally produced EPO has various metabolic effects as well as influence adipose tissue (Rundqvist et al., 2009).

## Exercise, acupuncture and myokines

Myokines may provide a conceptual basis for understanding how acupuncture may induce local effects within skeletal muscles during and after needling but also how EA especially may induce the release of myokines that communicate with other organs. This would suggest that exercise and EA might be an interesting treatment option, possibly also for prevention, in patients with diseases associated with inactivity like type 2 diabetes, cardiovascular diseases, breast and colon cancer, postmenopausal problems, dementia and depression (Bays, 2009; Giovannucci, 2007; Whitmer et al., 2008; Xue and Michels, 2007). Without doubt there is a major overlap between several diagnoses, which points at the possibility that although these disorders have very different phenotypical presentations, they share some underlying pathogenic mechanisms.

It is well known that both physical inactivity and abdominal adiposity are associated with persistent systemic low-grade inflammation (Yudkin, 2007; Festa et al., 2002; Handschin and Spiegelman, 2008). Models of lipodystrophy suggest that if the subcutaneous fat becomes inflamed and adipocytes undergo apoptosis/necrosis, the fat storing capacity is impaired and fat will

consequently be deposited as ectopic fat (Caron-Debarle et al., 2010). One obvious explanation to the differential outcome of accumulating fat subcutaneously or as ectopic fat could be that when fat is stored in 'the wrong places', it will stimulate an inflammatory response (Yudkin, 2007). Evidence exists that visceral fat is more inflamed than subcutaneous fat and constitutes an important source of systemic inflammation. In this respect it is interesting to note that acupuncture may have an anti-inflammatory effect and that exercise may be recommended in the protection against diseases associated with chronic inflammation, including rheumatic diseases (Gleeson et al., 2011; Mathur and Pedersen, 2008; Benatti and Pedersen, 2015). A hypothetical scenario could be that each bout of exercise or EA session induces an anti-inflammatory reaction, as muscle-derived IL-6 inhibits TNF production and stimulates the production of the anti-inflammatory cytokines IL-1 $\beta$  and IL-10. Exercise and EA probably have pleiotropic positive effects in almost every organ system, potentially having myokine-mediated direct and indirect anti-inflammatory effects in inflammatory diseases. As part of the effects of exercise that are locally mediated, local needling (muscle points around the knee) and EA stimulation, inducing visible contractions, should be advocated when treating low-grade inflammatory conditions like knee osteoarthritis. This would also suggest that distant needling or manual acupuncture is suboptimal and superficial needling even more so.

## Concluding comments

The overall clinical effects of acupuncture may be attributed to

- release of adenosine, NO and CGRP in peripheral tissue by axonal and dorsal root reflexes
- modulation of sympathetic tone and motor reflexes in the spinal segments
- modulation of activity in the descending pain inhibitory and facilitatory systems starting in the supraspinal region of the CNS
- change in the brain's functional connectivity; deactivation of limbic structures and the HPA axis; change in the function of the prefrontal and frontal cortex as well as the somatosensory cortex
- restoration of the brain's default mode connectivity
- modulation of the balance between the sympathetic and parasympathetic nervous systems
- modulation of function in the immune system
- activation of connective tissue
- activation of muscles and the release of myokines
- context dependent effects including verbal information, non-verbal interaction with the therapist (the therapists' ability to be compassionate, mediate empathy and give consolation) and expectations.

Taken together there are specific peripheral effects of acupuncture (neural, muscle, connective tissue and/or immunological) that may be therapeutic. To obtain such effects the stimulation technique and site must be adapted to the condition treated.

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# Neuroimaging: a window into human brain mechanisms supporting acupuncture effects

V. Napadow ■ N.W. Kettner ■ R.E. Harris

## CHAPTER OUTLINE

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## Introduction

The brain exerts control over all functional subsystems within the body (e.g. cardiorespiratory, renal, musculoskeletal, endocrine, etc.) and helps regulate homeostatic balance. The wide range of physical effects exerted by acupuncture and its purported efficacy for a compendium of clinical pathologies suggests that the brain may be responsible for transducing the needle stimulus into signals aimed at maintaining homeostatic balance within and across functional subsystems. Neuroimaging methods such as functional magnetic resonance imaging (fMRI), positron emission tomography (PET), electroencephalography (EEG), magnetoencephalography (MEG) and proton magnetic resonance spectroscopy (<sup>1</sup>H-MRS) provide unique means to probe the brain mechanisms, both functional and neurochemical, supporting clinically relevant acupuncture effects in humans.

While the neuroscientific exploration of acupuncture has mainly used animal models, most of the techniques involved are too invasive to perform on humans. This is a major limitation to our understanding of how acupuncture works. For example, though animal research clearly supports a role for anti-nociceptive limbic and brainstem networks in acupuncture analgesia (for review see [Han, 1998](#); [White, 1999](#); [Takeshige, 2001](#)), it is difficult to know how these findings may be operative in humans which display more complex neurobiological behaviours. Acupuncture is likely to be more than just the direct somatosensory afference (information transferred to the brain from the periphery via the nervous system) afforded by the needle. How patients anticipate, perceive and re-evaluate acupuncture needling in the context of the patient-practitioner relationship, that is its salience and behavioural relevance, are likely to be critical components underlying acupuncture's therapeutic effects. Human research is necessary to answer these questions, and recent applications of neuroimaging to explore acupuncture effects in humans have opened a window to the brain mechanisms supporting both needling and more complex whole treatment effects (see reviews: [Dhond et al., 2007a,b](#); [Beissner and Henke, 2011](#); [Huang et al., 2012](#)).

Neuroimaging spans a broad range of technologies that can map or localise function, evaluate brain morphometry, and investigate neurotransmitter activity. Functional neuroimaging technologies such as PET, fMRI, MEG/EEG, and  $^1\text{H}$ -MRS provide a means to monitor the neurophysiological effects of acupuncture in the human brain. Techniques such as fMRI and PET are most useful for localising cortical and subcortical (e.g. thalamic, basal ganglia, cerebellar and brainstem) brain activity. In contrast, because of their excellent temporal resolution, EEG/MEG are better suited for determining the temporal sequence of activity within the active brain. Finally, neurotransmitter activity can also be assessed with PET, as well as  $^1\text{H}$ -MRS. These imaging modalities are complementary, as they assess different aspects of the human brain, answering different research questions.

This chapter will review neuroimaging evidence informing our understanding of brain mechanisms supporting acupuncture therapy. While substantial acupuncture research has demonstrated anti-nausea and anti-emetic effects, most acupuncture research, both animal and human, has focused on analgesic effects. Neuroimaging research has similarly focused on analgesia and anti-nociception. This chapter will be organised by neuroimaging modality – fMRI, MEG/EEG, PET and  $^1\text{H}$ -MRS. Each sub-section will contain a brief review of the imaging technology, followed by its application to acupuncture research. Understanding the possibilities and limitations of each technology is critical in evaluating existing research and designing future research projects to inform our understanding of acupuncture. Neuroimaging has been used to both characterise evoked brain response to acupuncture needling, as well as assess longitudinal changes in brain activity in response to acupuncture therapy. The latter approach has been termed ‘translational research’, as it incorporates mechanistic research into a clinical trial-like framework, where questions of efficacy can be answered in conjunction with questions of mechanism.

## **fMRI: mapping brain response to acupuncture**

fMRI is the most commonly applied method of functional neuroimaging and has been applied to evaluate acupuncture in well over 100 studies (Huang *et al.*, 2012). It relies on the hemodynamic ‘blood oxygenation level dependent’ (BOLD) effect, which reflects the ratio between oxygenated and deoxygenated haemoglobin (Kwong *et al.*, 1992; Ogawa *et al.*, 1992). The BOLD contrast is used to infer which areas of the brain are active and may be used to map response within superficial as well as deep areas of the brain. This includes limbic, cerebellar and even brainstem areas all putatively involved in therapeutic acupuncture. BOLD fMRI has relatively good spatial resolution ( $1\text{--}3\text{ mm}^3$ ) and does not involve the hazards of ionising radiation. However, it has limited temporal resolution due to the delay and temporal spread of the hemodynamic response which is thought to peak 4–5 s after neuronal activity (Rosen *et al.*, 1998).

Different experimental designs can incorporate fMRI measurements. For instance, event-related and block designs have been commonly used to assess brain response to acupuncture needle stimulation. In recent years, fMRI data has been used to assay brain inter-regional connectivity, which has been investigated during specific brain states such as at wakeful rest, sleep, cognitive task performance and even acupuncture stimulation. Both the former (task-related activation) and latter (state-specific connectivity) approaches will be considered later.

Characterisation studies have used fMRI to evaluate brain response to needle stimulation. Brain response to needle insertion is more difficult to assess as fMRI relies on averaging brain response to multiple events in order to achieve a statistically robust signal, while the number of times it is practical to insert a needle in the same location during an experimental session is limited. In general, acupuncture point specificity is historically an important aspect of traditional acupuncture theory. One form of acupuncture point specificity lies in the somatotopic response in the primary somatosensory cortex (i.e. the S1 homunculus) (Nakagoshi *et al.*, 2005). This brain

region is well known for neurons that preferentially respond to tactile stimulation from different body areas. However, the spatial resolution of fMRI (i.e. mm) precludes evaluation of the precision by which acupuncture points are historically defined. In other words, fMRI can be used to distinguish S1 response to tactile stimulation of the back versus the hand, or even adjacent fingers (Napadow et al., 2006), but not acupuncture points LI4 versus LI3, for example. In addition to S1, some fMRI data suggest that acupuncture given at traditional ‘vision-related’ acupuncture points elicits activity primarily within the visual (occipital) cortex (Cho et al., 1998; Li et al., 2003). However, such acupuncture point specificity has been controversial and has not been replicated (Gareus et al., 2002; Parrish et al., 2005; Cho et al., 2006). For instance, a study suggests that occipital cortex response to acupuncture stimulation is not unique to vision-related acupuncture points and instead reflects known cross-modal communication between the somatosensory and visual systems in the brain (Kong et al., 2009a).

### Clinical points

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Stimulation of different acupuncture points elicits overlapping responses within multiple cortical, subcortical/limbic and brainstem areas.

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A meta-analysis (Huang et al., 2012) of 34 studies investigating fMRI response to acupuncture needle stimulation found that while statistical and methodological concerns pervaded, echoing a prior review (Beissner and Henke, 2011), brain response to acupuncture needle stimulation was characterised by a common pattern of activation and deactivation (Fig. 4.1). Stimulation of different acupuncture points elicits overlapping responses within multiple cortical, subcortical/limbic and brainstem areas (Hsieh et al., 1998; Wu et al., 1999; Hui et al., 2000; Yoo et al., 2004; Napadow et al., 2005, 2009a,b; Pariente et al., 2005). This includes primary and secondary somatosensory cortices (SI, SII), which support initial localization and early qualitative characterisation of somatosensory stimuli. Limbic brain regions (e.g. hypothalamus, amygdala, cingulate, hippocampus) are also recruited. The hippocampus and amygdala putatively support learning and memory while the amygdala may also play a dominant role in affective encoding (i.e. mood) (Zald, 2003). Both structures are directly connected to the brainstem as well as the hypothalamus, which modulates neuroendocrine and homeostatic function. Coordinated interaction between the amygdala/hippocampus and the hypothalamus may affect arousal and motivational state. In general, many components of the limbic system are down-regulated in response to acupuncture (Wu et al., 1999; Hui et al., 2000, 2005; Napadow et al., 2005), specifically if *deqi* sensation is induced.

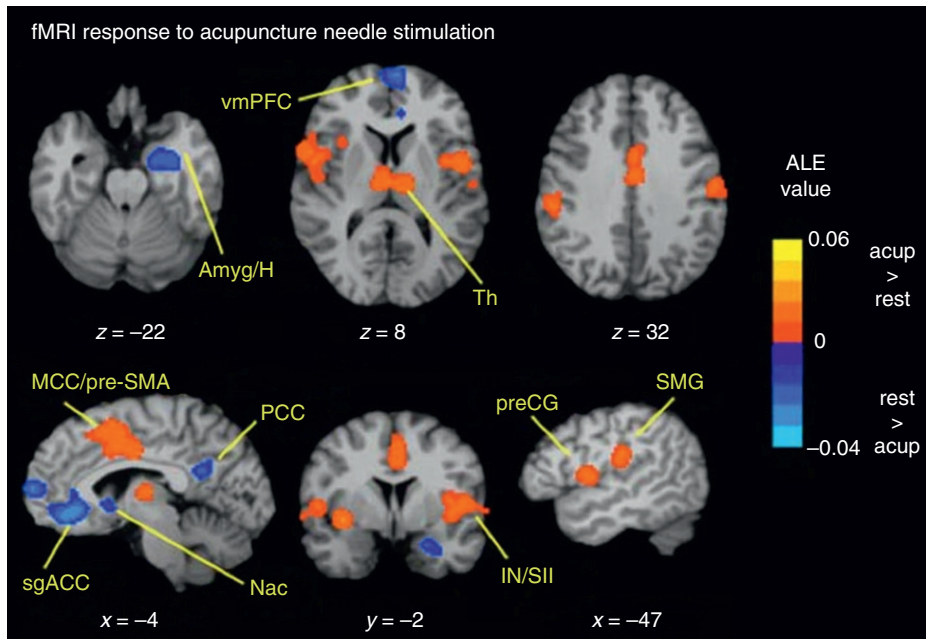
### Clinical points

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Many components of the limbic system are down-regulated in response to acupuncture, specifically if *deqi* sensation is induced.

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Furthermore, many acupuncture studies have demonstrated modulation of anterior and posterior insula, and the prefrontal cortex (PFC). The insula has been implicated in the sensory-discriminative dimension of visceral pain (Peyron et al., 2000) and may also play a role in therapeutic acupuncture (Pariente et al., 2005). Finally, the PFC, which has multiple distributed connections with the limbic system, is likely to play an important role in expectancy related modulation of pain processing (Casey, 1999). Several of the regions mentioned previously, particularly the insula and cingulate, have also been shown to support peripheral autonomic response to acupuncture (Beissner et al., 2012; Napadow et al., 2012b), while dorsomedial prefrontal areas may specifically support *deqi* sensation (Napadow et al., 2009a,b). While comparisons to sham



**Figure 4.1** A meta-analysis of 34 fMRI studies characterising brain responses to acupuncture found a common response pattern across studies where somatosensory (S1, S2, thalamus) and stimulus salience (insula, mid-cingulate) regions were activated, while affective limbic (amygdala, Nac, DMN) regions were deactivated. Note: amygd, amygdala; DMN, default mode network; fMRI, functional magnetic resonance imaging; IN, insula; MCC, middle cingulate cortex; Nac, nucleus accumbens; PCC, posterior cingulate cortex; sgACC, subgenual anterior cingulate cortex; SII, secondary somatosensory cortex; SMA, supplementary motor area; SMG, supramarginal gyrus; Th, thalamus; vmPFC, ventromedial prefrontal cortex. (Reproduced from Huang, W., Pach, D., Napadow, V., Park, K., Long, K., Neumann, J., et al., 2012. Characterizing acupuncture stimuli using brain imaging with fMRI – a systematic review and meta-analysis of the literature. *PLoS One* 7 (4), e32960.)

acupuncture have been less common, Huang et al. in their meta-analysis found evidence of greater insula and mid-cingulate activation and greater amygdala deactivation in response to real compared to sham acupuncture (Huang et al., 2012). Ultimately, knowing the brain regions that activate or deactivate in response to acupuncture stimulation can aid in formulating more specific hypotheses that are based on our extensive, and growing, understanding of the functional significance underlying activity in different brain regions.

While many of the previously mentioned ‘characterisation’ or ‘poke and look’ neuroimaging studies have mapped brain response during acupuncture stimulation, other studies have explored the effects of acupuncture immediately following stimulation – e.g. how brain response to a pain stimulus is altered by prior acupuncture stimulation. Studies in healthy adults demonstrate similar fMRI signal reduction to pain within the sensory thalamus, anterior cingulate cortex and premotor cortex after acupuncture stimulation at either real or sham (non-classical) acupuncture points (Cho et al., 2002). Another study found that expectancy mediates the brain circuitry underlying evoked pain analgesia following acupuncture in healthy subjects. While high expectation coupled with either real or sham acupuncture produced analgesia of similar magnitude, real acupuncture produced greater fMRI signal decrease in pain-related brain regions (Kong et al., 2009b).

Other studies have found that resting brain connectivity is also modulated by acupuncture (Dhond et al., 2008b; Liu et al., 2009). Resting functional connectivity MRI (fcMRI) is an

adaptation of fMRI that examines intrinsic connectivity – defined as ongoing neural and metabolic activity that occurs in the resting basal state. Intrinsic brain connectivity may be important for maintenance of synaptic connectivity and as such modulates the efficiency and extent of neuronal transmission between brain regions. Intrinsic connectivity, as measured by neuroimaging methods, follows known structural monosynaptic and polysynaptic pathways (Krienen and Buckner, 2009; van den Heuvel et al., 2009), likely reflecting meaningful neurophysiological activity (Raichle, 2009) within known primary sensory, executive and associative networks (Fox and Raichle, 2007). fMRI investigations are conducted with subjects simply resting in the scanner. Such state-specific measures have been linked with neurocognitive performance and even spontaneous pain (Napadow et al., 2010) in different patient populations. Additionally, studies have found that real, but not non-penetrating sham acupuncture, increased resting default mode network (DMN) connectivity immediately after needling (Dhond et al., 2008a). This result suggests that even after the needling procedure, there are sustained effects on brain activity. In fact, brain regions comprising the DMN, such as posterior cingulate, inferior parietal and especially medial prefrontal cortices, have been linked to chronic (and not evoked, experimental) pain perception (Baliki et al., 2008; Napadow et al., 2010). Hence, acupuncture modulation of DMN connectivity has important clinical implications as a potential mechanism of analgesic response.

### Clinical points

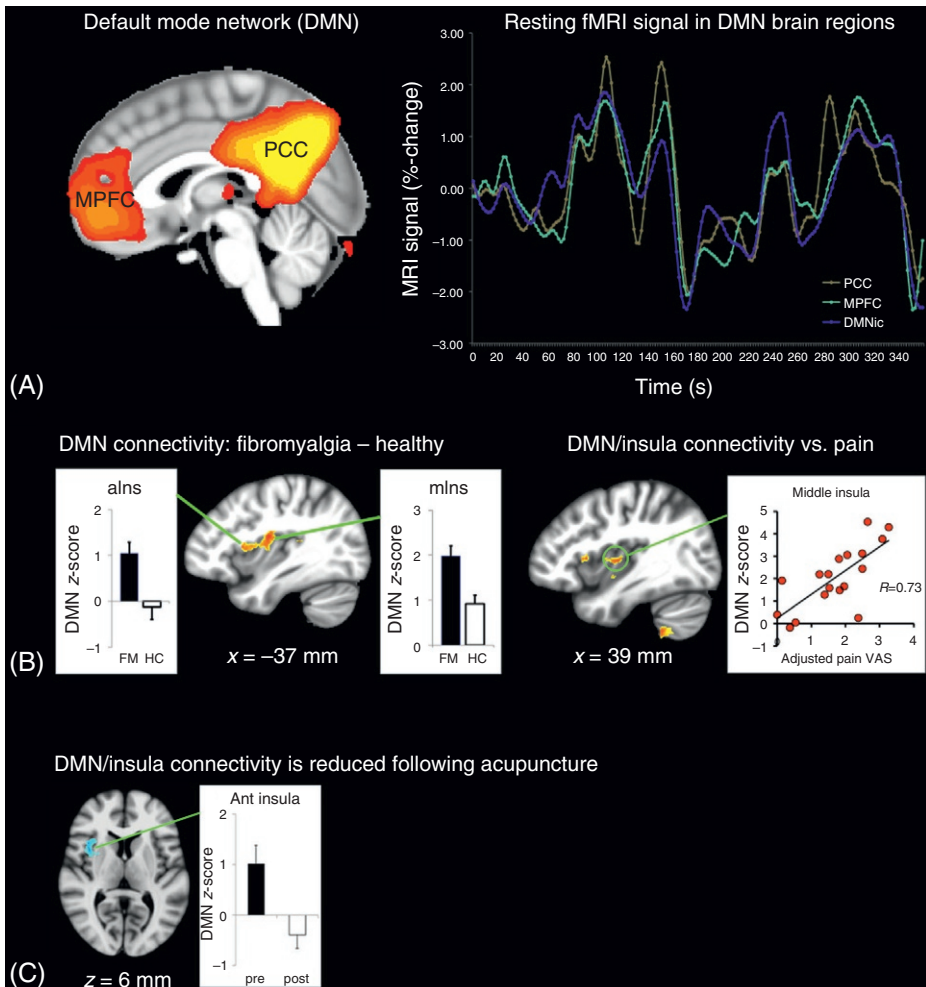
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Acupuncture modulates DMN connectivity, which is likely to be relevant to treatment of chronic pain.

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Importantly, fMRI can also be incorporated into a longitudinal clinical trial-like design. Evaluation can occur at baseline and after a multi-week course of clinical acupuncture. For instance, studies with carpal tunnel syndrome (CTS) patients demonstrated that pain and paraesthesia coincided with sensorimotor hyperactivation and an overlapping or blurred representation of adjacent fingers within S1 (Napadow et al., 2006). Following a 5-week course of acupuncture treatment, there was clinical improvement, partial release from hyperactivation, and more somatotopically separated finger representations (Napadow et al., 2006). Improvement in SI finger separation was correlated with improvement in peripheral median nerve electrophysiological measures. Brain response to acupuncture stimulation in CTS has also been associated with abnormal median nerve conduction (Maeda et al., 2013a), and was shown to predict analgesia following stimulation – a predictive approach for acupuncture neuroimaging study design (Maeda et al., 2013b).

Other examples include evaluation of resting fMRI connectivity before and after a longitudinal course of acupuncture therapy. At baseline chronic pain patients diagnosed with fibromyalgia (FM) displayed greater resting connectivity between the DMN and insula (Fig. 4.2) – a brain region activated by evoked experimental pain and acupuncture (Apkarian et al., 2005; Huang et al., 2012). Furthermore, greater spontaneous pain at the time of the scan was associated with greater intrinsic connectivity between the insula and DMN. Napadow et al. went on to show that a longitudinal course of manual or sham acupuncture (with somatosensation), given to these same FM patients, was able to diminish pain and decrease DMN–insula connectivity (Napadow et al., 2012a,b). Given the immediate effects of acupuncture on resting DMN connectivity mentioned previously (Dhond et al., 2008a,b), it is conceivable that a short-term increase in connectivity between the DMN and anti-nociceptive regions such as the periaqueductal grey are linked with long term diminished DMN connectivity in pain processing areas such as the insula. Similar experimental designs should continue to be applied and have demonstrated similar DMN modulation after acupuncture in chronic low back pain (Li et al., 2014). Such research has promise in identifying potential brain mechanisms underlying clinically relevant effects in clinical patient populations.



**Figure 4.2** Acupuncture modulates resting brain connectivity in chronic pain patients. **(A)** Functional magnetic resonance imaging (fMRI) can be used to assess resting functional connectivity within and between different brain regions and networks, such as the default mode network (DMN), where fMRI signal between the medial prefrontal cortex (MPFC) and posterior cingulate cortex (PCC) is highly correlated. **(B)** Chronic pain patients suffering from fibromyalgia (FM) have increased resting DMN connectivity to the insula, and this connectivity is greater with greater pain reported at the time of the scan (Napadow et al., 2010). **(C)** Acupuncture (both sham and verum) were found to reduce pain and reduce DMN/insula connectivity (Napadow et al., 2012a,b).

## MEG and EEG: spatio-temporal response to acupuncture

EEG measures the change in electrical potentials over the scalp surface during various tasks. Cortical as well as deep brain structures can produce such potentials, and electrical activity can arise from either neuronal and/or glial cells in the brain (Nunez, 1990). MEG, in contrast, evaluates changes in weak magnetic fields measured just outside of the head. These fields are thought to reflect post-synaptic potentials within the dendrites of cortical pyramidal cells (Hamalainen and Hari, 2002).

MEG is more sensitive to superficial compared to deep sources of synaptic activity because the strength of the neuronal magnetic field decreases as a function of radial distance away from the source. Both EEG and MEG have excellent temporal resolution (ms) but relatively limited spatial resolution (>1 cm) due to an ill-posed inverse problem of trying to localise the exact spatial location of activity using data coming only from the surface (Dale and Halgren, 2001).

Most MEG/EEG somatosensory studies utilise paradigms in which trials of sensory stimuli are repeated. Thus when averaging trials, brain responses which are time-locked to the stimulus (i.e. occur at the same time following each stimulus event) become visible against the background noise. Spectral analysis is another common MEG/EEG analysis method that is often used to quantify signals on the basis of the amount of 'frequency power' present in different frequency bands (i.e. alpha, beta, gamma, theta, delta, etc.). Both approaches have been applied to study acupuncture, and will be discussed later.

MEG and EEG studies have made important contributions in evaluating the temporal dynamics of the somatosensory components of acupuncture. EEG studies have demonstrated that electroacupuncture (EA) modulates median nerve somatosensory evoked potentials (SEPs) due to sensory interference (Yamauchi et al., 1976a,b). MEG studies have also found that evoked responses for EA and non-penetrating tapping at acupuncture point PC6 are both localised to the contralateral SI cortex (Dhond et al., 2008a,b; Witzel et al., 2011). However, EA demonstrated different adaptation of beta band desynchronization, while initial response to non-penetrating tapping peaked at longer poststimulus latencies (~35 ms) than EA (~20 ms) due to temporal dispersion caused by the mechanical (vs. electrical) mode of stimulation. These important distinctions could also inform differences between manual and EA.

### Clinical points

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Manual and EA elicit different brain responses.

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MEG/EEG studies have also investigated cognitive effects of acupuncture, suggesting that analgesia may be mediated or modulated by attention mechanisms. For example, one study compared the effects of fentanyl, nitrous oxide ( $N_2O$ ), and low frequency EA stimulation on experimental pain and found that all three treatments decreased the amplitude of the SEP P250 pain-related component (Chapman et al., 1980). The authors thus suggested that acupuncture analgesia may be based on attentional mechanisms. However, a different study comparing low frequency EA with desflurane anaesthesia on noxious abdominal stimulation was unable to find any significant effects of EA (Chernyak et al., 2005). Another EEG study compared verum versus sham EA in subjects given propofol anaesthesia and found a significant decrease in the P260 pain SEP after real but not sham EA (Meissner et al., 2004). The authors then reasoned that acupuncture analgesia was not related to changes in attention since both groups were sedated. Such variability in findings may be due to differences in the strength, nature and region of stimulation and the pain model used. Furthermore, acupuncture analgesia that occurs in the context of acute experimental pain may be mediated by different mechanisms than when it occurs in the clinical pain setting (i.e. chronic pain treated with multiple intervention sessions).

### PET and $^1H$ -MRS: mapping brain and neurotransmitter and receptor response to acupuncture

While fMRI and MEG/EEG methods provide relatively good temporal and spatial resolution, they yield very little information about the underlying neurochemical and cellular processes involved in acupuncture and sham acupuncture procedures. With regard to these questions, PET

and  $^1\text{H}$ -MRS may be more appropriate tools. Specifically PET can be used to assess changes in neurotransmitter levels as well as receptor binding properties in living awake humans. However, PET requires the use of radioactive molecules (tracer or ligand), which bind to specific receptors involved in neurotransmission (e.g.  $^{11}\text{C}$ -carfentanil binds to the mu-class of opioid receptors,  $^{18}\text{F}$ -fluoroethylspiperone binds to dopamine receptors). A significant advantage of this imaging modality is that, depending on the tracer, one can explore specific neurotransmitter activities. PET is considered 'minimally invasive', and due to its use of ionising radiation, the number of scans an individual may undergo over a given period of time is limited. Furthermore, while the spatial resolution in PET can be as good as  $8\text{ mm}^3$ , the temporal resolution, being on the order of minutes, is too low to investigate neuronal mechanisms of the brain in real-time (Aine, 1995). However, in applications exploring brain response to acupuncture therapy with analgesic effects peaking hours, if not days, after a treatment (Price et al., 1984), PET may be very advantageous as it assesses long-term or slower changes in brain activity.

As an example, Harris et al. investigated the action of verum and sham acupuncture on mu-opioid receptor (MOR) binding in chronic pain patients diagnosed with FM (Harris et al., 2009). Previous work, arising largely from studies in animals, suggested that endogenous opioids and their associated receptors were involved in acupuncture analgesia (Pomeranz and Chiu, 1976; Pert et al., 1981; He et al., 1985; Ho and Wen, 1989; Chen et al., 1996). Most of these studies revealed that enhanced opioid neurotransmitter release accompanied needle insertion (Stux and Hammerschlag, 2001). However less attention has been paid to the opioid receptors themselves (e.g. the mu, kappa and delta opioid receptor classes) and their relationship with clinical response. Since placebo administration also induces activation of opioid receptors, specifically the MOR class (Levine et al., 1978; Benedetti and Amanzio, 1997; Amanzio and Benedetti, 1999; Zubieta et al., 2005), it has been hypothesised that acupuncture may indeed operate in part via placebo mechanisms (i.e. in this context via expectation). However using PET imaging of dynamic changes in MOR binding with the radiotracer  $^{11}\text{C}$ -carfentanil, Harris et al demonstrated that the action of verum and sham acupuncture on MOR binding was different: sham acupuncture caused a decrease in MOR binding ability (consistent with previous placebo studies), whereas verum acupuncture increased receptor binding ability within the same brain regions. Moreover, in the verum group, those individuals that displayed a greater increase in MOR binding ability were the very same patients that had improvements in clinical pain. Interestingly, while clinical pain was reduced to a similar extent in the verum and the sham group, the MOR mechanisms by which this occurred were markedly different. Similar effects of verum acupuncture on opioid receptor binding have also been demonstrated in animal models (Gao et al., 1997) and another trial in humans with the non-specific opioid receptor radiotracer diprenorphine (Dougherty et al., 2008). While these findings are provocative, it should be noted that the sample sizes used in these PET studies were small ( $n=20$  or less), typical of most neuroimaging studies. Future studies should also investigate if these findings can be replicated in other pain states.

## Clinical points

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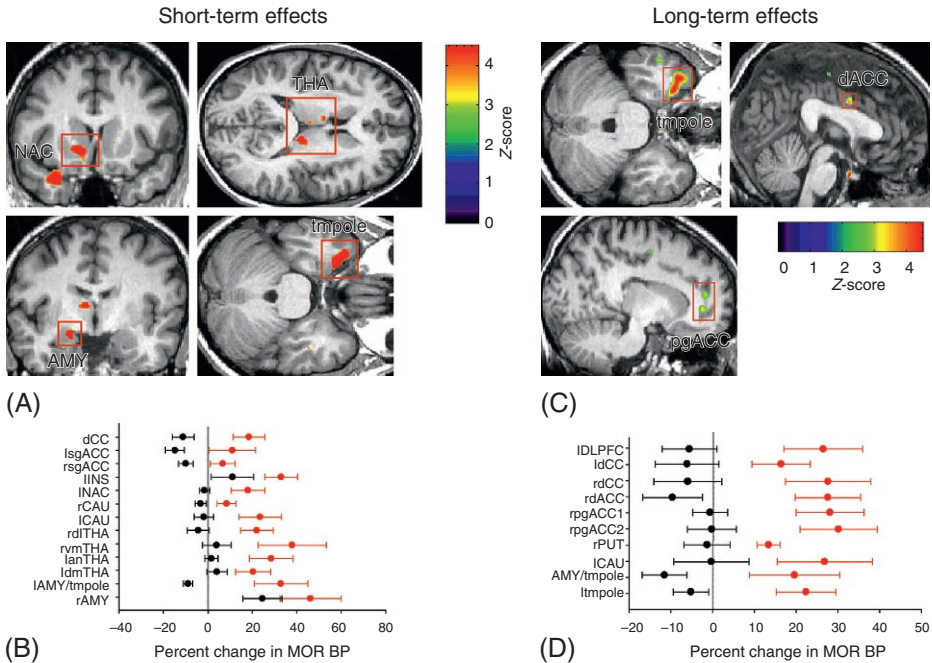
Studies suggest that real acupuncture increases opioid receptor binding ability while sham acupuncture reduces it.

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Other PET approaches to evaluate brain physiology in response to acupuncture utilised non-specific PET ligands, which yielded data similar to fMRI – i.e. investigated haemodynamics as a proxy for neural activity. An interesting study used this PET approach to explore brain response to verum versus sham (Streitberger needle) needling (Pariente et al., 2005) and found that verum acupuncture induced greater brain response in the ipsilateral insula compared to sham. Consistent with fMRI data mentioned previously, this type of neuroimaging study is demonstrating that

verum and sham acupuncture may indeed have divergent brain mechanisms implying that acupuncture and sham/placebo acupuncture are not equivalent on a physiological level, even when they produce similar clinical outcomes in randomised controlled trials (Fig. 4.3).

Another neuroimaging modality which can evaluate neurotransmitter activity is  $^1\text{H}$ -MRS, a non-invasive magnetic resonance imaging (MRI) technique that quantifies the concentration of multiple metabolites, including the brain's major excitatory and inhibitory neurotransmitters, glutamate and gamma aminobutyric acid (GABA) respectively, within the living human brain. Rather than obtaining a spatial map of brain activity over time, as in traditional fMRI and PET, this technique generates a chemical specific spectrum by exciting protons with characteristic resonance frequencies (de Graaf, 1998).  $^1\text{H}$ -MRS methods are amenable to both cross-sectional as well as longitudinal studies, as specific regions of interest can be identified between subjects as well as within the same participant over time. Once  $^1\text{H}$ -MRS spectra are acquired, they can be analysed to determine the relative concentrations of different central nervous system metabolites. Historically these metabolites have been: *N*-acetyl-aspartate, choline and creatine as these molecules displayed a good signal to noise ratio (Provencher, 1993; de Graaf, 1998). Abnormalities in the concentrations of these metabolites have been associated with various



**Figure 4.3** Differential short-term and long-term effects of acupuncture and sham acupuncture on MOR binding potential (BP). **(A)** Regions of interest showing increased MOR BP following acupuncture as compared to sham treatment. *Upper left:* left nucleus accumbens (INAC), *upper right:* three thalamic regions (THA), *lower left and right:* left amygdala (IAMY) and temporal pole (ltmpole), respectively. **(B)** Short-term percent changes in MOR BP for all regions identified. Red circles (TA) and black circles (SA) represent group mean values with standard error bars. Overall acupuncture resulted in increases in MOR BP with sham treatment resulting largely in either no change or small decreases in BP. **(C)** Regions of interest showing long-term increased MOR BP following acupuncture as compared to sham treatment. *Upper left:* temporal pole (ltmpole), *upper right:* dorsal anterior cingulate cortex (dACC), *lower left:* two perigenual anterior cingulate regions (pgACC). **(D)** Percent changes in MOR BP for all regions identified. Red circles (TA) and black circles (SA) represent group mean values with standard error bars. Overall acupuncture resulted in long-term increases in MOR BP whereas sham treatment resulted in either no change or a decrease in binding ability.

pathological changes in the underlying brain tissue.  $^1\text{H-MRS}$  has been used widely to better characterise brain disorders such as depression (Yildiz-Yesiloglu and Ankerst, 2006a,b), bipolar disorder (Yildiz-Yesiloglu and Ankerst, 2006a,b), schizophrenia (Marsman et al., 2011) and epilepsy (Hetherington et al., 2002); however, the application of  $^1\text{H-MRS}$  to the investigation of chronic pain and interventions such as acupuncture has been slow in coming.

Glutamate is the brain's main excitatory neurotransmitter and it exerts its effects via binding to both ionotropic and metabotropic receptors (Kandel et al., 2000). We have known for some time that glutamatergic neurotransmission plays a key role in symptoms of pain. For example the development of neuropathic pain in preclinical models is thought to be in part a result of central sensitization, or central plasticity, involving both ionotropic as well as metabotropic glutamate receptors (for review see Latremoliere and Woolf, 2009). Interestingly, acupuncture is also thought to change synaptic plasticity (Napadow et al., 2007; Xing et al., 2007), which may involve changes in the glutamatergic system. Harris et al. used  $^1\text{H-MRS}$  to study glutamate and combined glutamate + glutamine (Glx) levels specifically in patients with FM that were treated with acupuncture (Harris et al., 2008). In a longitudinal trial, wherein patients were treated with either verum or sham acupuncture, he demonstrated significant correlations between changes in glutamate (and Glx) within the posterior insula cortex and changes in both experimental and clinical pain: patients with greater reductions in glutamate and Glx displayed greater improvements in both clinical and experimental pain outcomes. These changes in insular Glx were also associated with concomitant changes in fMRI activity evoked by painful stimulation, highlighting the possibility that changes in Glx are associated with changes in neural activity.

## Clinical points

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Changes in glutamate levels correlate with changes in pain scores during acupuncture treatment.

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Another investigation explored the use of  $^1\text{H-MRS}$  in assessing fat content levels in children with elevated BMI (Zhang et al., 2011). This open label magnetic resonance spectroscopy (MRS) imaging trial found that acupuncture significantly reduced abdominal visceral and total body fat. More studies are needed to evaluate acupuncture mechanisms in humans, and more studies are needed to examine the effects of acupuncture versus sham therapy on neurotransmitter systems such as Glu and GABA.

## Concluding comments

In conclusion, neuroimaging has proven to be an important research tool for acupuncture that can bridge the gap between invasive basic science research using animal models and clinical trials research using human patients. By linking physiological response in the human brain with clinical outcomes, neuroimaging studies can aid future animal research studies in choosing more appropriate mechanistic models to test. Human neuroimaging studies can also aid future clinical trials by, for example, identifying patient biomarkers at baseline that might predict response to acupuncture treatment for a given disorder. Clinical prediction models could facilitate optimal patient selection and maximise the efficiency of an acupuncture dose in a clinical trial. Future research will also need to take advantage of novel experimental designs and multimodal applications of multiple neuroimaging techniques to further probe potential brain mechanisms supporting different therapeutic acupuncture effects. Finally, combining neuroimaging data with more rigorous computational models, including chaos theory and nonlinear dynamics, to study acupuncture treatments may offer important insights into the complexity of the multifactorial framework of health and disease related to brain dynamics (Siegelmann, 2010).

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# Neurophysiology of chronic pain

R. Gupta ■ P. Farquhar-Smith

## CHAPTER OUTLINE

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## Introduction

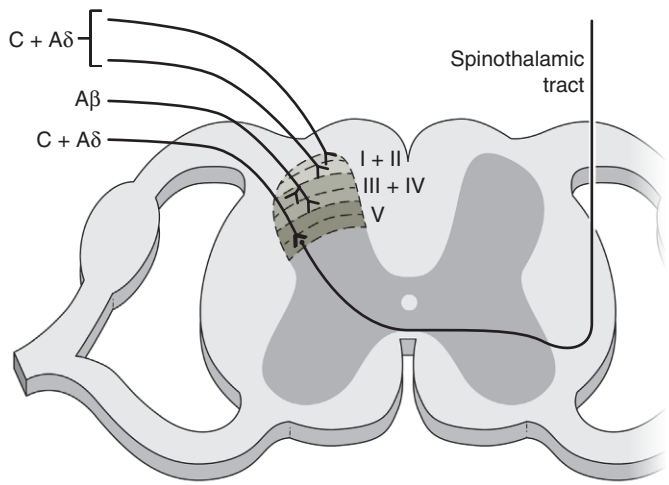
Pain is an unpleasant sensory experience associated with actual or potential tissue damage. The point at which acute pain becomes chronic is arguable but most definitions state between 3 and 6 months from the onset of pain. The acute to chronic transition is mediated by alteration of nerve function by peripheral and central sensitisation. Persistent pain can result in anxiety and depression and affect quality of life.

Nociceptive information is transmitted by nociceptors to the cerebral cortex and is processed by a specialised pathway: the nociceptive pathway. The nociceptive system consists of pathways passing the information from the periphery to dorsal horn and ascending to the midbrain and thence the cortex. Descending pathways also exert major influences on this system. These pathways are modulated at many levels that can change their function (plasticity).

## Classification of pain

Pain may be nociceptive, that is, caused by activation of nociceptors by sensory stimuli. Nociceptors can also become hypersensitive consequent to inflammation or nerve injury (neuropathic pain) (Woolf and Costigan, 1999a,b). Neuropathic pain is caused by a lesion or dysfunction in the peripheral or central nervous system and may be somatic or visceral.

Pain can also be categorised as somatic or visceral (Fig. 5.1). Somatic pain arises from tissues (skin, muscles, joints, bones and ligaments) and is often sharp and well localised although some somatic pains (e.g. muscle pain) can also present as more dull and less well localised. Visceral pain arises from internal organs of the main body cavities, e.g. myocardial pain, biliary colic.



**Figure 5.1** Primary afferent neuron terminations in the dorsal horn.

Organisation of pain pathways

The pathway for pain and its modulation comprises nociceptors and dorsal horn neurons, ascending and descending pathways, and also the ‘pain matrix’ involving many areas of midbrain and cortex.

NOCICEPTORS

Nociceptors are primary afferent neurons which are involved with initial perception of pain. They are found in skin, muscles, joints (somatic) and viscera (Willis and Coggeshall, 1991). Nociceptors can be classified according to the type of pain sensation transmitted or according to their conduction velocity (Table 5.1).

Some nociceptors are normally silent (i.e. they show no activity) but are recruited by mediators of inflammation which are released secondary to injury. A large proportion of visceral afferents appear to be silent. Visceral inflammation can induce a large increase in their activity in afferent pain transmission.

TABLE 5.1 ■ Features of somatic and visceral pain

	Somatic nociceptive pain	Visceral nociceptive pain
Localisation	Accurate localisation in skin Less well defined in muscle	Poorly localised
Quality	Sharp (skin) Muscle duller	Dull, diffuse, cramping
Autonomic symptoms	Rare	Frequent
Trigger	Tissue damage On occasion, ischaemia	Ischaemia, inflammation, contraction, distension
Referred pain	Yes – refers to other somatic areas	Yes – but typically refers to somatic areas

Primary afferent nociceptors synapse with second order neurones in the superficial dorsal horn of the spinal cord. Dorsal root ganglia (DRG) contain the cell bodies of these afferents.

Primary afferent nociceptive neurons can be distinguished biochemically. One group is dependent upon glial cell derived neurotrophic factor for development and expresses P2X3 purine receptor and IB4 lectin binding site. These afferents terminate in deeper parts of the substantia gelatinosa (lamina II inner) (Silverman and Kruger, 1988; Snider and McMahon, 1998). Others are nerve growth factor (NGF)-dependent and express peptides such as calcitonin-gene-related peptide (CGRP) and terminate superficially in the dorsal horn (lamina I and II outer) (Averill et al., 1995).

DORSAL HORN

The grey matter containing the cell bodies of the second order neurones is divided into 10 Rexed laminae (Rexed, 1952). The most superficial layer is called the marginal zone or Lamina I which receives input from small diameter afferent fibres (Aδ and C fibres). Lamina II or substantia gelatinosa is involved with sensation of heat and pain. Laminae IV–V form the deep dorsal horn which receives input from large diameter Aβ fibres and small diameter C fibres. See Table 5.2. The majority of the neurons in lamina V are wide dynamic range (WDR) cells as they respond to both low and high threshold stimuli (Price, 1988). Somatic information is carried in second order neurones that decussate before ascent to the brain in tracts. Visceral nociception is processed in many areas including lamina V and the central region of the spinal cord, lamina X. These areas contain interneurons and projection cells that communicate with dorsal column nuclei and other brain areas conveying visceral pain. The visceral nociceptive input carried by the dorsal horn remains uncrossed and is then relayed with the crossed medial lemniscal fibres to the thalamus (Willis et al., 1979). Excitatory and inhibitory interneurons are important mediators of local modulation of nociceptive processing (Chung et al., 1984).

TABLE 5.2 ■ Properties of C and Aδ fibres

Morphology	C (Unmyelinated, <1.3µm diameter)	Aδ (Thinly myelinated, 1–5µm diameter)
Dorsal root ganglia (DRG) cells	Small	Small
Function (Konietzny et al., 1981; Ochoa and Torebjork, 1989)	‘Slow’ pain	Mostly sharp pain
Stimulus	Polymodal	Thermal/mechanical
Conduction velocity (Gasse, 1950; Boivie and Perl, 1975)	<3m/s	5–30m/s

There are several ascending pathways that transmit information to the brain stem and higher centres. However there are also descending pathways from areas of the brain that can have profound effects on the modulation of pain processing at the level of the spinal cord.

ASCENDING PATHWAYS

*Spinothalamic projection:* Neurons project from the dorsal horn and give rise to axons that decussate and ascend within the lateral funiculus to form the spinothalamic tract. The neurons from this tract project to areas of the thalamus and then third order neurons project to the primary sensory somatosensory area. This projection plays a role in arousal and motivational responses to painful stimuli. The neurons are predominantly WDR neurons and respond to a broad range of stimulus intensity. There are also nociceptive specific neurons which respond to painful stimuli only.

*Spinomesencephalic tract:* Neurones in lamina I, IV–VI and X project to the midbrain via the spinomesencephalic tract (Wiberg et al., 1987). The neurons are nociceptive. Projections to periaqueductal grey (PAG) contribute to aversive behaviour (Nashold et al., 1969).

*Dorsal column pathways:* These are formed by the axons of second order projection neurons located in Lamina III–IV and some from X. The axons project to dorsal column nuclei of medulla oblongata. They respond to input from muscle, skin, joints and cutaneous afferents and transmit information of various noxious visceral stimuli to the thalamus such as after mechanical and chemical irritation of viscera (Al-Chaer et al., 1996a,b).

*Spinolimbic tracts:* These are multiple tracts conveying noxious stimulus to the medial thalamus, where it is relayed to the limbic system. The neurons respond to noxious mechanical stimuli and visceral stimuli. Some projections relate to the affective component of pain (Burstein and Giesler, 1989).

## DESCENDING PATHWAYS

The descending pathways regulate the pain either facilitation or inhibition depending upon the neurotransmitter associated with that pathway.

The PAG area of the mesencephalon is an area in the midbrain which plays an important role in emotion and pain (Merker, 2007). Its stimulation causes inhibition of nociceptive dorsal horn neurons, including spinothalamic tract cells via rostroventral medulla (RVM), producing significant analgesia mediated by spinal 5-HT receptors and  $\alpha 2$  adrenoreceptors (Yaksh, 1979). The PAG receives inputs from many nuclei in the thalamus, hypothalamus and brainstem. Important projections are rostroventromedial pathway, locus coeruleus and cell groups of lateral reticular nucleus and nucleus tractus solitarius.

The nuclei of RVM (rostral ventromedial pathway) include the nucleus raphe magnus and some parts of the reticular formation. Increased sensitivity to painful stimuli (hyperalgesia) triggers the RVM (Ren and Ruda, 1996). Its processing mechanisms are involved with the maintenance of neuropathic, central and visceral pain (Burgess et al., 2002). Electrical stimulation of the nucleus raphe magnus produces strong antinociception that can be reversed by naloxone (Oliveras et al., 1977). The neurons involved in the pathway are classified into three types based on their response to noxious stimuli. 'On cells' which are activated by a noxious stimulus, 'Off cells' which exhibit inhibitory activity on stimuli (Heinricher et al., 1994) and neutral cells which do not show any activity.

The locus coeruleus lies near the reticular system and has direct axonal connections with the spinal cord. The stimulation of this area inhibits responses to noxious somatic stimuli primarily mediated by  $\alpha 2$  adrenoreceptors (Jones and Gebhart, 1986). Other important brain stem areas include the lateral reticular nucleus, the stimulation of which inhibits spinal nociceptive reflexes (Gebhart and Ossipov, 1986). In addition the nucleus tractus solitarius can modulate pain to noxious heat (Morgan et al., 1989) and other C fibre-evoked responses.

## CENTRAL PROCESSING AND THE 'PAIN MATRIX'

Central processes are important in final processing of the noxious stimuli and involve brainstem, hypothalamus, thalamus and cortex. The cortical and sub cortical regions are associated with pain processing. Important areas involved are anterior cingulate gyrus, insula, frontal cortices, primary and secondary somatosensory cortex and amygdala. They form the 'Pain Matrix' (Ingvar, 1999). The matrix is divided into medial and lateral regions. The lateral system comprises of somatosensory area I and II and is involved in location and intensity of painful stimuli (Kanda et al., 2000). There are several other important brain stem structures thought to be involved in pain processing such as the reticular formation (Bowsher, 1976), the gigantocellular and magnocellular areas of medial reticular system (Kasey, 1971) and the posterior part of ventral medial nucleus

(Craig, 2003). Damage to the lateral thalamic nuclei (which receive nociceptive input) results in significant impairments in pain localisation (Ploner et al., 1999).

The anterior cingulate cortex is involved with the affective component of pain, and the insula is involved with localisation, affective-motivational and cognitive aspects of pain (Melzack and Casey, 1968). Damage to the insula does not influence the pain threshold (Berthier et al., 1988) but reduces the affective component of pain, referred to as pain asymbolia (Greenspan et al., 1999). Moreover, functional imaging has shown pain related activation in anterior parts of the insula (Tolle et al., 1999). The cingulate gyrus appears to be involved in pain processing and receives input from the medial thalamic nuclei (Sikes and Vogt, 1992). The amygdala also has a role in pain (Bornhovd et al., 2002), especially pain associated with fear, anxiety and depression.

The hippocampus is situated in the deep medial temporal lobe and is important in pain processing and learning related behaviour. It is important in chronic pain and chronic pain related avoidance behaviour (Ploghaus et al., 2000).

## BIOCHEMICAL MEDIATORS OF PAIN PROCESSING

Chemical mediators are involved in processing of pain. Excitatory neurotransmission is predominantly mediated by the excitatory amino acids such as glutamate and aspartate. Glutamate is present in the synaptic vesicles of most afferent terminals. Various other neurotransmitters contribute to excitation including CGRP, substance P and other neurokinins. Inhibitory neuropeptides include galanin and somatostatin.

The excitatory amino acids act on ligand-activated ion channels. There are three principal types:  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA receptors), *N*-methyl-D-aspartate (NMDA) receptors, and kainite (KA) receptors. Activation of AMPA receptors increases sodium ion inflow (Gouaux, 2004), whereas the NMDA receptors are nonselective and allow permeability to both sodium and calcium channels (Paoletti and Neyton, 2007). In the acute setting, AMPA is the main transmitter, but after development of central sensitisation, the NMDA receptors become more important. Magnesium ions block the NMDA receptors until released by increased stimuli from peripheral sensitisation. KA channels are ligand-activated ion channels that have a role in pain processing by modulation of gamma aminobutyric acid (GABA) release (Rodriguez-Moreno and Sihra, 2007).

*Substance P* is located in small diameter primary afferents and is released following cutaneous noxious stimuli (Harrison and Geppetti, 2001). It is mainly seen in Lamina I and II. It acts by binding to NK1 receptors on second order neurons affecting intracellular G-protein related phosphorylation, modifying the gain of nociceptive transmission. In persistent inflammatory states, substance P and NK1 activation occurs but there is significant up regulation of NK1 receptors in lamina 1 neurons. This leads to prolonged opening of the NMDA channel leading to increased calcium entry which further potentiates glutamate transmission adding to central sensitisation (Yoshimura and Yonehara, 2006).

CGRP is a common peptide in the afferent system which has a role in nociceptive processing (Van Rossum et al., 1997). It regulates nociceptive responses by promoting the release of substance P and glutamate from primary afferents, while also impeding the metabolism of substance P (Allen et al., 1999). CGRP alone causes a slow membrane depolarisation in sensory neurons and an influx of calcium through voltage-gated calcium channels (VGCCs), enhancing sensitisation and promoting NK1 and NMDA activation.

*Serotonin* (5HT): the main serotonin receptor associated with nociception is 5HT<sub>3</sub>, which is a ligand-gated ion channel (Farber et al., 2004). Local damage-induced serotonin release can activate nociceptors and enhance the response of nociceptors to bradykinin. 5HT<sub>2</sub> receptors are expressed largely in CGRP containing small diameter neurons and their activation produces thermal hyperalgesia (Abbott et al., 1996). 5HT<sub>2</sub>-mediated depolarisation of capsaicin sensitive DRG neurons reduces resting potassium conductance and leads to sensitisation (Todoriv and Anderson, 1990).

## Neuroimmune interactions

### CENTRAL

Non-neuronal cells involved in pain processing include immune cells, and the central nervous system (CNS) counterparts such as astrocytes and microglia. After tissue injury and inflammation, circulating cytokines can activate perivascular astrocytes and microglia. Injury and inflammation will lead to acute and chronic activation of microglia and astrocytes (Watkins et al., 2001). Cytokines regulate nitric oxide (NO) by interfering with the production of nitric oxide synthase (NOS). Astrocytes produce two forms of NOS – inducible and constitutive – whereas microglia are responsible for inducible NOS (iNOS) (Xiao and Link, 1998). Tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) and interleukin-1 $\beta$  (IL-1 $\beta$ ) control the stimulation of iNOS in both astrocytes and microglia. Glial cells have been implicated as important in the central/spinal mechanisms of certain types of neuropathic pain (Zhuo et al., 2011).

### PERIPHERAL

Inflammation is triggered by innate immune activation of pattern recognition receptors including Toll like receptors (TLRs) that recognise and bind invading pathogens or endogenous molecules released from damaged cells, such as heat shock proteins and high mobility group box 1 protein (Guo and Chluesener, 2007). TLRs are expressed in immune cells, including monocytes or macrophages and dendritic cells and in immune related cells such as keratinocytes. Binding to TLRs is followed by activation of nuclear factor- $\kappa$ B signalling and release of inflammatory cytokines. Immune cells, mast cells and macrophages are also activated after injury and release proinflammatory cytokines, chemokines, effectors of the complement cascade (C3a and C5a) and vasodilators, including vasoactive amines and bradykinin. Blood borne neutrophils, monocytes and T lymphocytes adhere to the vessel walls, extravasate and accumulate at the site of injury. These immune cells contribute to peripheral nociceptive sensitisation by releasing soluble factors and interacting directly and indirectly with nociceptors.

Mast cells are found in close proximity to primary nociceptive neurons and contribute to nociceptor sensitisation in a number of contexts. Mast cell degranulation also contributes to rapid onset of NGF-induced thermal hyperalgesia (Lewin et al., 1994). Mast cells not only express the trkA NGF receptor, but degranulation releases NGF along with many other proinflammatory mediators. Histamine has an important role in mediating mast cell induced nociceptor activation (Rudick et al., 2008).

Macrophages are increased at the site of injury and are involved with the development of mechanical allodynia (Cui et al., 2000). Macrophages contribute to nociceptor sensitisation by releasing several mediators. Expression of the chemokine macrophage inflammatory protein 1 $\alpha$  and the receptors CCR1 and CCR5 is increased in macrophages after partial ligation of the sciatic nerve and contribute to the development of neuropathic pain (Kiguchi et al., 2010). Neutrophil migration is also associated with inflammatory pain (Ting et al., 2008). Lymphocytes contribute to the sensitisation of peripheral nociceptors. T cells infiltrate the dorsal root ganglion after nerve injury and mice lacking T cells do not show hyperalgesia and allodynia (Moalem et al., 2004). The complement system also has a role in inflammatory hyperalgesia and neuropathic pain. C5a is involved in neuropathic pain as it activates spinal microglia in neuropathic pain and blockade of the complement system in spinal cord reverses neuropathic pain behaviour (Twining et al., 2005).

### OTHER MEDIATORS

Bradykinin is involved in pain signalling. The bradykinin receptor B1 is involved in chronic pain while the B2 receptor is involved in acute inflammation and pain (Couture et al., 2001). Bradykinin is released from tissues after injury and via the B2 receptor causes release of substance

P and CGRP from primary sensory neurons. B2 receptor antagonists eliminate bradykinin-induced excitation of nociceptors in inflamed tissue (Banik et al., 2001). Similarly histamine release is enhanced by substance P which can excite polymodal visceral nociceptors and potentiates the response of nociceptors to bradykinin and heat (Mizumura et al., 1995).

Many cytokines are released after noxious stimuli including IL-6, IL-1 $\beta$  and TNF $\alpha$ . They play an important role in modulating pain by directly or indirectly influencing nociceptors. The sensitisation seen in the acute nociceptive phase is due to activation of kinases associated with receptors and ion channels whereas transcriptional alterations of nociceptors are mainly seen in chronic inflammation (Kidd and Urban, 2001). TNF $\alpha$  induces ectopic activity in nociceptive afferent fibres and evokes C fibre activity by decreasing the mechanical threshold in nociceptors (Sorkin et al., 1997). IL-6 can sensitise the nociceptors to heat (Obreja et al., 2002). IL-1 $\beta$  promotes spontaneous discharge and hyperalgesia and increases peripheral receptive fields to mechanical stimulation (Fukuoka et al., 1994).

Matrix metalloproteinases (MMPs) are extracellular proteases comprising collagenases, stromelysins and gelatinases. TNF $\alpha$  is a potent inducer of MMP gene expression (Nagase, 1997). MMPs are involved with nociception by release of cytokines (Kobayashi et al., 2008). Inhibition of MMPs is an important approach to cytokine related neuropathic pain.

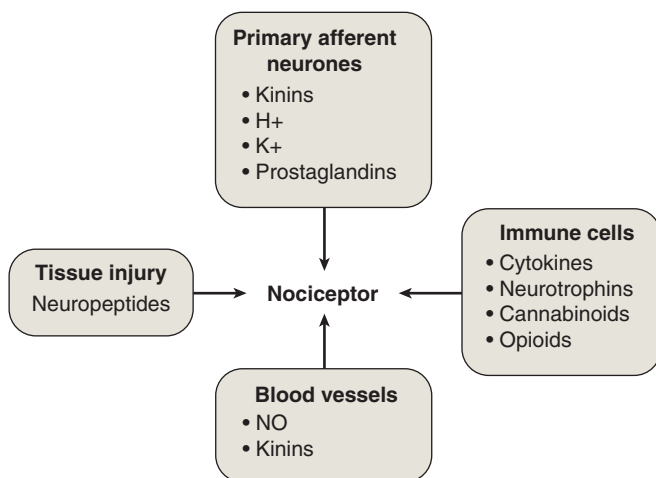
## Mechanisms of pain processing

Noxious stimuli are converted to an electrical signal (signal transduction) resulting in generation of an action potential (transformation). Mitogen activated protein kinases are thought to be involved in transduction. Ion channels involved in mechanical transduction include transient receptor potential vanilloid type 4 (TRPV4), acid sensing ion channel 3, and the low threshold VGCC, CaV3.2. Following noxious stimuli, there is an increase in density of several transducers and post-translational modifications. This increases channel activity or sensitivity such that transducers are activated by lower intensity stimuli. Noxious stimuli also lead to alteration in the action potential threshold and spike initiation to increase the excitability of nociceptive neurons. The main ion channel involved in the action potential is the voltage-gated sodium channel, NaV1.6. After nerve damage, an increase in sodium channels is seen causing instability of membranes, which in chronic conditions may cause the neurons to become source of ectopic activity.

## PERIPHERAL SENSITISATION

A key factor involved in inflammatory changes is NGF. NGF recruits macrophages via secretion of chemokines. Macrophage-mediated release of the cytokine IL-1 $\beta$  leads to increased expression of NGF thus activating and sensitising nociceptors (Kanaan et al., 1998). NGF also produces sensitisation by altered gene expression and posttranslational regulation of receptors and ion channels. Systemic administration of NGF leads to sensitisation of C fibre afferents and pain behaviour in animal models (Thomson et al., 1995).

Sensitisation is a characteristic feature of nociceptors; non-nociceptors do not become sensitised following tissue insult. Sensitisation of nociceptors results in primary hyperalgesia. Nociceptor sensitisation can be induced via sensitisation of transduction channels or a decrease in the threshold of sodium channels responsible for spike initiation (Devor, 2006). In neuropathic pain, nerve damage leads to macrophage infiltration, T cell activation and increased expression of proinflammatory cytokines. TNF $\alpha$  can activate nociceptors and TNF $\alpha$  blockers can attenuate the development of hyperalgesia after nerve damage (Schafers et al., 2003). This leads to a lower discharge threshold and increased spontaneous discharge of nociceptors (Li et al., 1999). The frequency of nociceptor discharges is increased with expansion of the receptor field (Nurmikko, 2000). See Figure 5.2 for the mechanisms involved in inflammation and nociceptor sensitisation.



**Figure 5.2** Mechanisms involved in inflammation and nociceptor sensitisation.

Sensitisation is mediated by a plethora of mediators which directly or indirectly activate nociceptors. Nociceptor specific receptors include TRPV1 and TRPM8 (transient receptor potential cation channel subfamily M member 8 or menthol receptor), and are involved with thermal stimuli. NGF expression is increased after lesion and is involved in sensitisation of the receptors by direct activation. Many of these members of the ‘inflammatory soup’ mediate their effects through second messengers such as cyclic adenosine monophosphate (cAMP), PKA and PKC (protein kinase A and C) which induce sensitising changes that are at least in part mediated by ion channels. The resulting primary sensitisation leads to an increase in afferent input to the spinal cord. This increased afferent barrage induces many changes resulting in increased excitability of central neurons. Many dorsal horn neurons are sensitised following nociceptor sensitisation leading to enhanced or facilitated synaptic transmission (Dubner and Ruda, 1992).

## CENTRAL SENSITISATION

Central sensitisation (also known as secondary sensitisation) leads to several clinical manifestations including non-noxious stimuli causing pain (allodynia) and noxious stimuli resulting in an augmented pain response (hyperalgesia) and duration (hyperpathia). An increase in the pain receptive field is also seen whereby tactile allodynia and increased pain sensitivity can be demonstrated in the uninjured area surrounding the damaged tissue (Torebjorkn et al., 1992).

Central sensitisation may involve homosynaptic or heterosynaptic mechanisms. Homosynaptic mechanisms involve direct afferent stimulus from the site of injury whereas the heterosynaptic mechanism involves input from intact afferents. Both sensitisations occur due to increased release of transmitters and increased synaptic efficacy. These changes seen are due to:

*Presynaptic mechanisms:* this is due to augmented release of glutamate. Normally there is inhibition of glutamate presynaptically by several metabotropic protein G-protein receptors, e.g.  $\mu$  opioid receptors. Nerve injury causes down regulation of  $\mu$  opioid receptors (Kohno et al., 2005) and up regulation of  $\alpha 2\delta$  subunit of VGCCs in the DRG and spinal cord (Li et al., 2004) leading to enhanced release of glutamate.

*Postsynaptic mechanisms:* increased afferent input from peripheral sensitisation and subsequent changes at the level of the spinal cord leads to aberrant opening of NMDA voltage-gated channel leading to increased calcium entry (Duggan, 1995). The NMDA receptors are

normally blocked by magnesium ions, and on depolarisation the magnesium ion is replaced by glutamate which activates a kinase cascade potentiating neuronal fibre sensitisation. An increase in expression of other glutamate activated receptors is seen in the superficial dorsal horn after nerve lesion leading to further sensitisation (Harris et al., 1996).

*Interneuron changes:* various changes following noxious stimuli are seen in the interneurons, including a decreased expression of inhibitory receptors and down regulation of K-Cl channel transporter KCC2. The latter effect contributes to hyperalgesia (Coull et al., 2003).

Different forms of central sensitisation are seen:

*Wind up:* this is a form of homosynaptic plasticity, manifest by a progressive increase in action potential output from dorsal horn neurons seen as a result of low frequency C fibre or nociceptive stimuli (Mendell, 1984). There is excessive release of the neuropeptides substance P and CGRP which activates postsynaptic G protein coupled receptors, leading to postsynaptic depolarisations (Woolf and Salter, 2000). These depolarisations further recruit VGCCs thus triggering a cycle of depolarisation and recruitment. However, wind up is a specific response to repetitive stimuli and should not be used synonymously with central sensitisation.

*Heterosynaptic sensitisation:* this is an immediate onset, activity dependant increase in the excitability of nociceptive neurons in the dorsal horn of the spinal cord (McMahon and Wall, 1984). This can cause low threshold sensory fibres to activate high threshold nociceptive neurons by light stimuli, i.e. allodynia. This sensitisation is apparent within seconds of the painful stimulus and can last for hours. The sensitisation manifests itself in a reduction in threshold required to cause pain due to recruitment of low threshold A $\beta$  fibre input and also an increase in the extent of receptive fields of the dorsal horn (Woolf and Salter, 2000). Neurotrophins (such as brain derived neurotrophic factor (BDNF)) and cytokines like TNF $\alpha$  (released from glial cells) can enhance synaptic transmission (Watkins et al., 2001).

NMDA receptors are expressed in the dorsal horn and are necessary for induction of central sensitisation. There is an increase in NMDA receptor function and an exponential increase in influx of calcium/calmodulin dependant kinase II and phosphorylation of the AMPA receptor subunit protein GluR1, which causes AMPA channels to persist in a high conductance state causing long term potentiation (Malinow and Malenka, 2002).

The central sensitisation associated with tissue injury produces transcriptional changes in primary sensory and dorsal horn neurons, altering their function for prolonged periods (Woolf and Costigan, 1999a,b). Any noxious stimulus or inflammation increases expression of the immediate early genes c-fos and COX-2 and late response genes prodynorphin, NK1 and TrkB in dorsal horn neurons (Hunt et al., 1987). All these genes contain cyclic AMP response element sites in their promoter regions, and the ERK/CREB (extracellular signal regulated kinase/cAMP element binding protein) pathway may mediate induction of these CRE (cAMP response element) containing genes. Blocking ERK activation reverses these transcriptional changes and the development of a late onset spinal cord component of postinflammatory hypersensitivity (Ji et al., 2002). After both peripheral inflammation and nerve injury, a phenotypic switch is seen in some dorsal horn neurons which begin to express substance P and BDNF (Neumann et al., 1996), making central sensitisation more likely.

Another mechanism contributing to sensitisation is the rearrangement of synaptic contacts. Tactile mechanical allodynia after peripheral nerve injury is mediated by low threshold myelinated A $\beta$  fibre afferents (Campbell et al., 1988). There is recruitment of A $\beta$  fibre input into nociceptive specific cells during central sensitisation (Woolf and King, 1990). Also following a lesion to a peripheral nerve, the central axons of injured myelinated A $\beta$  fibres sprout from their normal site of termination in the deeper laminae of dorsal horn (lamina II and IV) into lamina II of the dorsal horn violating the normal laminar topography of their projections and entering terminal areas normally restricted to C fibre and A $\delta$  nociceptors (Kohama et al., 2000). Nerve injury can cause disruption of the glial sheath allowing electrical and chemical cross connection between adjacent

neurons (Amir and Devor, 2000). A $\beta$  fibres may directly activate C fibres so that non-noxious stimuli can produce pain. Although this has been robustly demonstrated in animal models, there is some debate as to whether these processes occur in humans.

## Concluding comments

The physiology of pain is becoming clearer with research in basic science. Research has also provided us with the understanding potentially to develop novel approaches to manage acute and chronic pain. The pain system can be visualised as a complex array of pathways and a network of systems but with the ability to make numerous neuroplastic changes, constantly affecting processing. The changes in the sensitivity of the nociceptor and its connections (both peripheral and central) are pivotal to pain processing and are mediated by a myriad of compounds and neuroimmune interactions. The development of the notion of the 'pain matrix' has illustrated the key role of pain processing in higher centres of the brain and the interaction of areas that colour the emotional, discriminative, cognitive and overall experience of pain.

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# Acupuncture and the autonomic nervous system

E. Stener-Victorin

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## Introduction

The autonomic nervous system (ANS) is, together with the endocrine system, an important homeostatic system with the main function of regulating and controlling visceral organs. The ANS consists of the sympathetic and the parasympathetic parts. The regulation of visceral organs is mainly mediated via two different routes (Sato et al., 1997). First, changes in emotions, consciousness or circadian rhythm result in activation of autonomic efferent nerve fibres and may result in increased heart rate and blood pressure, sweating and increased skeletal muscle blood flow in preparation for exercise. Second, regulation of visceral organs is mediated via reflexes from peripheral sensory receptors – visceral, somatic and cranial receptors. Information from these receptors is transmitted to the central nervous system (CNS) and modulates the activity and function in the autonomic efferents to the organ. Increased knowledge of the regulation of the so-called somato-autonomic reflexes has increased our understanding of the mechanisms of physical therapies, including acupuncture. Importantly, somato-autonomic reflex centres are located both in the spinal cord and brain (Sato et al., 1997). Also, it is important to keep in mind that different organ systems may react differently and may be regulated either via spinal reflexes or supraspinal reflexes or both. As an example, the urinary bladder is mainly regulated via spinal reflexes while the heart is mainly regulated by supraspinal reflexes, although both reflexes are dependent on the segmental areas stimulated (Sato et al., 1997).

The close interaction between the somato-autonomic reflexes and the endocrine system has to be stressed. As an example, the adrenal sympathetic efferent nerve activity controls catecholamine secretion from the adrenal medulla, and the pancreatic sympathetic and parasympathetic efferent nerve activity controls insulin secretion from pancreas (Higashimura et al., 2009). Further, ovarian sympathetic nerves are involved in the regulation of ovulation and secretion of sex steroids (Barria et al., 1993).

This chapter will focus on how acupuncture may modulate autonomic function with examples from different organ systems.

## Mechanisms by which acupuncture modulates the autonomic function

Intramuscular needle insertion and stimulation cause a particular pattern of afferent activity in peripheral nerves (Kagitani et al., 2005). Various fibre types, thick myelinated (A $\beta$ ), thin myelinated (A $\delta$ ) and thinner unmyelinated C fibres have all been reported to be excited by acupuncture needle stimulation (Sato et al., 2002). After insertion, acupuncture needles are stimulated by manual manipulation and/or by electrical stimulation, so-called electroacupuncture (EA), for 20–40 min. During EA, needles are attached to electrodes for passing an electric current. It has been suggested that low-frequency (1–15 Hz) EA with repetitive muscle contraction activates physiological processes similar to those resulting from muscle contraction during physical exercise (Andersson and Lundeberg, 1995; Kaufman et al., 1984).

Stimulation of acupuncture points in muscle tissue causes peripheral release of a number of neuropeptides, such as substance P (SP), calcitonin gene related peptide (CGRP), vaso-intestinal peptide (VIP) and nerve growth factor (NGF), from peripheral nerve terminals into the surrounding area. The result is increased microcirculation in skeletal muscle (Sato et al., 2000) and glucose uptake, the latter most likely via a reflex response from muscle twitches during manual or electrical stimulation (Higashimura et al., 2009).

Depending on the number and location of acupuncture needles and the intensity and type of stimulation, activation of muscle afferents also modulates the transmission of signals in the spinal cord (segmental level) and in the CNS (Stener-Victorin et al., 2008). Through sympathetic reflexes, acupuncture at the segmental (spinal) level may modulate the function of organs (e.g. ovaries, urinary bladder and heart) located in the same innervation area as the stimulated acupuncture points (Sato et al., 1997). Simultaneously, the nervous system transfers signals to the brain, which generates a response that may further influence the organ. Both segmental (spinal) and central mechanisms of acupuncture most likely contribute to the total effect of acupuncture treatment. Since the CNS regulates the release of hormones from the pituitary, acupuncture may also modulate the endocrine system which in turn may affect the activity in the sympathetic nervous system.

Specifically, low-frequency EA causes the release of a large number of neuropeptides, serotonin, endogenous opioids and oxytocin in the CNS, which seem to be essential for inducing functional changes in different organ systems (Andersson and Lundeberg, 1995; Han, 2004; Stener-Victorin et al., 2008). Of particular interest is  $\beta$ -endorphin, an endogenous opioid with high affinity for the  $\mu$ -receptor (Basbaum and Fields, 1984). The central hypothalamic  $\beta$ -endorphin system has a regulatory role in a variety of functions, including autonomic function (Andersson and Lundeberg, 1995; Eyvazzadeh et al., 2009).  $\beta$ -endorphin is produced and released from the arcuate nucleus in the hypothalamus and the nucleus tractus solitarius in the brain stem, which project to a number of sites within the brain, including all parts of the hypothalamus (Ferin et al., 1984).  $\beta$ -endorphin is a key mediator of changes in autonomic functions, such as effects on the vasomotor centre, which results in a general decrease of sympathetic tone, shown as regulation of blood pressure and as decreased muscle sympathetic nerve activity (MSNA) (Andersson and Lundeberg, 1995; Yao et al., 1982).

$\beta$ -Endorphin is also released into peripheral blood from the hypothalamus via the anterior pituitary (Crine et al., 1978), a process regulated by corticotropin-releasing factor (CRF), which is secreted from the paraventricular nucleus of the hypothalamus (Chan et al., 1982). CRF promotes the release of  $\beta$ -endorphin, adrenocorticotrophic hormone and melanocyte-stimulating hormone into the blood stream in equimolar amounts by stimulating the synthesis of their precursor, pro-opiomelanocortin.  $\beta$ -endorphin in plasma is thought to be related to the hyperinsulinaemia

response (Carmina et al., 1992) and stress (Lobo et al., 1983). It has been well documented that insulin can increase the sympathetic outflow, and it is suggested that hyperinsulinaemia may contribute to sympathetic overdrive in obesity (Gilchrist et al., 2006). Stress increases the activity of the hypothalamic-pituitary-adrenal (HPA) axis and decreases reproductive functions among many others. Thus, hormones of the HPA axis are closely related to those of the hypothalamic-pituitary-gonadal axis as well as sympathetic activity. As an example, menstrual disturbances and high circulating androgens in women with polycystic ovary syndrome (PCOS) are related to high activity in the sympathetic nervous system; see the succeeding text (Sverrisdottir et al., 2008).

Principles of point selection

When selecting points for regulation of a specific organ system, use the same somatic area as the organ. Table 6.1 gives examples of the location of preganglionic innervations of some organs (Bonica, 1990). In the Western medical acupuncture approach, the needles are placed in muscles and in somatic segments corresponding to the innervation of the target organ (see Table 6.1). Additionally, points are selected bilaterally, in the same innervations or in extra-segmental areas related to the organ in muscles of the arm below the elbow, to strengthen and prolong the effect on the CNS (Thomas and Lundberg, 1994; Thomas and Lundeborg, 1996). Although classical acupuncture points are not the only places where the nervous system can be stimulated, they are well described with respect to their anatomical location and innervations and are therefore often used in research. Classical acupuncture points are not specific and needling of non-acupuncture points in the same segmental innervations most likely causes similar effects.

TABLE 6.1 ■ Example of sympathetic and parasympathetic preganglionic innervation of organs that is likely to be modulated by acupuncture stimulation from needles placed in appropriate somatic area

Organ	Sympathetic preganglion innervation	Parasympathetic preganglion innervation
Heart	T1–4(5)	Nucleus motor dorsalis, n. vagus (X)
Lung and oesophagus	T2–6(7)	Nucleus motor dorsalis, n. vagus (X)
Gastrointestinal tract		
Stomach–duodenum	T(5),6–9,(10),(11)	Nucleus motor dorsalis, n. vagus (X)
Ilium–transverse colon	T8–12, L1–2	Nucleus motor dorsalis, n. vagus (X)
Descending colon–rectum		S2–4 (n. vagus (X)) <sup>a</sup>
Liver	T6–11	Nucleus motor dorsalis, n. vagus (X)
Pancreas	T6–11	Nucleus motor dorsalis, n. vagus (X)
Adrenal gland	T(7)8–L1(2)	
Kidney	T10–12, L1–2	Nucleus motor dorsalis, n. vagus (X)
Urinary bladder	T(11),12, L1–2	S2–4 (n. vagus (X)) <sup>a</sup>
Ovary and uterus	T(6–9),10–12, L1–2	S2–4 (n. vagus (X)) <sup>a</sup>

<sup>a</sup>Not completely verified.

## Measurement of autonomic activity

There are few optimal ways of measuring autonomic nerve activity. In humans, the gold standard method is microneurography that enables direct recording of sympathetic nerve activity to the vasculature of skeletal muscle, so-called muscle sympathetic nerve activity. The nerve activity is quantifiable and is typically reported as the number of bursts per minute, or as total nerve activity that takes into account the height of the bursts and the number of bursts per minute, or as total nerve activity that takes into account the height of the bursts and the number (Vallbo et al., 2004). Although it is a gold standard method, it is time consuming and requires skilled personnel to perform the procedures and analyse data.

Heart rate variability (HRV) measurements are based on continuous electrocardiographic (ECG) recording from which the time periods between heartbeats, identified as sinus depolarization (R–R-intervals), are derived. HRV is an indirect method that can be evaluated by different methods including time- and frequency-domain variables. The time-domain measurement includes statistical analyses of the variation in the beat-to-beat intervals and is used to estimate short-term (SDNN, the standard deviation of NN intervals and NN is used in place of RR to emphasise the fact that the processed beats are ‘normal’ beats; and RMSSD, the square root of the mean of the sum of the squares of the successive differences between adjacent NNs) or long-term (SDANN) variations obtained from 5 min to 24 h ECG recordings. The time-domain parameters are associated mostly with overall variability of HR over the time of recording, except RMSSD, which is associated with fast parasympathetic variability. SDNN reflects all cyclic components responsible for variability in the period of recording. The SDNN value clinically indicates the ANS's ability to maintain homeostasis against internal/external environmental challenges, coping ability to various emotional/physical stressors and general health. In the frequency-domain measurements three different spectral components can be distinguished: very low frequency, low frequency (LF) and high frequency (HF). The HF component represents the vagal control of heart rate, whereas LF component and the ratio LF to HF represent sympathetic modulation although the LF oscillations is controversial (Pomeranz et al., 1985). The LF/HF ratio is used to indicate balance between sympathetic and parasympathetic tone, thus, a decrease in this score might indicate either increased parasympathetic or decreased sympathetic tone. However, there is an ongoing dispute whether HRV is good index for autonomic regulation and the physiological relevance is not clear (Parati et al., 2006).

Further, markers of sympathetic nerve activity such as NGF, adrenergic receptors and urine norepinephrine (NE) are valuable but require tissue samples and are thus only available for research purpose.

## Effect of acupuncture on autonomic nerve activity

In healthy subjects, significant change in sympathetic and parasympathetic activity has been observed with different types of stimulation (Haker et al., 2000). For example, stimulation of the first dorsal interosseus (at LI4) decreased heart rate (mediated by sympathetic fibres) (Haker et al., 2000). A recent study on acupuncture for relief of migraine showed reduction of migraine attacks of at least 50%, and a reduction of the LF component of HRV, indicating decreased sympathetic activity (Backer et al., 2008). Further, stimulation of acupuncture needles has been shown to correlate with increased parasympathetic levels during stimulation and poststimulation and decrease in LF/HF ratio, indicating a normalising effect of acupuncture (Haker et al., 2000). Another study assessed the effect of acupuncture on HRV in patients with fatigue versus non-fatigue state and demonstrated a significant decrease in heart rate, LF power, total power and LF/HF ratio, indicating changes in autonomic activity (Li et al., 2005).

## HEART DISEASE

In patients with heart failure, MSNA is increased and patients with the highest sympathetic nerve activity have the poorest survival (Cohn et al., 1984). Although few human studies have studied whether acupuncture can decrease high sympathetic nerve activity in patients with heart failure, experimental studies in animals indicate that acupuncture decreases sympathetic nerve activity. Interestingly, the effect of acupuncture seems to be strongest in animal models with hypertension (Chao et al., 1999; Yao et al., 1982).

In one study, the acute effect of acupuncture was investigated in patients with advanced heart failure, and the major finding was that sympathetic activation during mental stress was eliminated after acupuncture at LI4, PC6 and LR3. However, one single treatment did not decrease sympathetic nerve activity in heart failure. In 2009 it was demonstrated that ten acupuncture treatments using a TCM approach over 5 weeks, 30 min per session with no stimulation, increase submaximal exercise capacity, ventilator capacity and recovery after exercise (Barres et al., 2009). In addition, HRV increased after acupuncture, which is a positive effect of autonomic function.

An increase in sympathetic nerve activity and alteration in arterial baroreceptor function appear to contribute to the pathogenesis of clinical hypertension. In experimental settings, acupuncture has been shown to decrease high blood pressure. In spontaneously hypertensive rats, low-frequency acupuncture stimulation, with intensity high enough to activate A $\delta$ -fibres for 30 min, produced an increased blood pressure during stimulation followed by a long-term reduction in blood pressure and in splanchnic nerve activity measured with microneurography (Yao et al., 1982). The effect was partially reversed by naloxone indicating that endorphin release was involved. Extensive experimental studies by the group of Longhurst et al. in animal models of hypertension have shown that the beneficial effects of acupuncture are associated with modulation of sympathetic outflow and possibly the endocrine system (de Lauzon et al., 2004). But the neuroendocrine mechanisms of acupuncture in the treatment of hypertension are not fully understood.

The major question is whether repeated acupuncture treatment has the potential to decrease blood pressure with a long-lasting effect. The biggest RCT in hypertensive patients compared three different acupuncture protocols with  $\leq 12$  treatments, twice weekly 30-min acupuncture sessions over 6–8 weeks (Macklin et al., 2006). All three protocols improved hypertension, although there were no differences between the different protocols, and the effect lasted  $\sim 6$  months. There are a number of other studies and also a systematic review indicating that acupuncture has beneficial effects on hypertension, but there is a need for more research (Lee et al., 2009).

## OBESITY AND INSULIN RESISTANCE

There is a relationship between obesity, insulin resistance and sympathetic activity (Gilchrist et al., 2006). Individuals with central obesity demonstrate augmented sympathetic outflow when compared to non-central obesity individuals. The underlying cause of high activity in the sympathetic nervous system in obesity is not fully understood, but it is likely to be multifactorial. The chronic increase in basal sympathetic nerve activity most likely aims to stimulate  $\beta$ -adrenergic thermogenesis to prevent further fat storage, but can also stimulate lipolysis to increase non-esterified free fatty acids, which in turn contributes to insulin resistance. Adipose tissue itself can act as an endocrine organ and express various adipokines, which may directly or indirectly increase sympathetic activity. A chronic increase in sympathetic outflow could in turn impair  $\beta$ -adrenergic signalling, reduce metabolism and progress to a vicious cycle contributing to obesity, insulin resistance and morphological changes in target tissues.

It is well documented that insulin can augment sympathetic outflow in animals, and it is suggested that hyperinsulinemia may contribute to the high activity of the sympathetic nervous system in obesity.

The clinical effect of acupuncture in obesity is not very well documented and will not be discussed in this chapter. However, with regard to changes in sympathetic activity in adipose

tissue, this has been studied in rats with dihydrotestosterone (DHT) induced PCOS. These rats are exposed to androgens from puberty and, compared with control rats, they develop obesity and insulin resistance and elevated mesenteric adipose tissue mRNA expression of beta-3 adrenergic receptor (ADRB3), NGF and neuropeptide Y (NPY), all markers of sympathetic activity (Manneras et al., 2009). In this animal model, repeated low-frequency EA decreased the mesenteric adipose tissue expression of ADRB3, NGF, NPY compared with untreated rats (Manneras et al., 2009). Interestingly, this regulation occurred in parallel with improved insulin sensitivity, but without affecting obesity.

Muscle contractions elicited by low-frequency EA also induce changes in skeletal muscle signalling pathways similar to changes induced by exercise (Atherton et al., 2005; Johansson et al., 2010; Liang et al., 2011). It has been demonstrated that glucose transporter 4 protein expression in skeletal muscle is increased, and it was mainly expressed in the membrane indicating translocation to the cell membrane (Johansson et al., 2010). These results indicate that acupuncture affects skeletal muscle signalling pathways but not whether this effect is mediated via modulation of sympathetic efferent activity or not. Interestingly, it has been demonstrated that when the afferent nerves in a treated hind limb were cut, the increased insulin responsiveness after electrical stimulation was lost, indicating the response is mediated by activation of afferent nerves rather than by the contractions *per se* (Higashimura et al., 2009); thus manual stimulation of acupuncture needles may induce a similar response.

## POLYCYSTIC OVARY SYNDROME

This is the most common endocrine and metabolic disorder of women in reproductive age and is associated with ovulatory dysfunction, hyperandrogenism and polycystic ovaries (see Chapter 32). Metabolic abnormalities include hyperinsulinaemia and type 2 diabetes, and obesity makes everything worse. The primary aetiology of PCOS is incompletely understood and remains a chicken-or-egg mystery despite the high prevalence of the syndrome. Ovarian hyperandrogenaemia, the most consistent endocrine feature, probably plays a key role (Abbott et al., 2002; Gilling-Smith et al., 1997), but hyperinsulinaemia and insulin resistance as well as abdominal obesity are also thought to be important etiological factors in PCOS (Barber et al., 2006; Dunaif and Thomas, 2001). Moreover, neuroendocrine defects can contribute to persistently rapid LH pulsatility and increased amplitude, which further augment ovarian androgen production (Blank et al., 2007).

Many factors associated with PCOS – disturbed central and peripheral  $\beta$ -endorphin release, hyperandrogenaemia, hyperinsulinaemia and insulin resistance, as well as abdominal obesity and cardiovascular disease – are also associated with increased activity in the sympathetic nervous system (Disson et al., 2009a; Fagius, 2003; Ojeda and Lara, 1989; Reaven et al., 1996; Sir-Petermann et al., 2002). The involvement of the sympathetic nervous system in PCOS pathology is further supported by the greater density of catecholaminergic nerve fibres in polycystic ovaries (Heider et al., 2001; Semenova, 1969). Increased ovarian sympathetic nerve activity might contribute to PCOS by stimulating androgen secretion (Greiner et al., 2005). Women with PCOS have enhanced ovarian production of NGF (Disson et al., 2009b), a strong marker of sympathetic nerve activity. These results suggest that overproduction of ovarian NGF is a component of PCO morphology in humans. In a transgenic mouse model overexpressing NGF in the ovaries, a persistent elevation in plasma LH levels was required for morphological abnormalities to appear (Disson et al., 2009b). The strongest evidence for an augmented sympathetic nervous system has been demonstrated in a microneurography study. It showed that women with PCOS have high sympathetic nerve activity that may be relevant to the pathophysiology of the syndrome (Sverrisdottir et al., 2008). Interestingly, testosterone was the strongest independent factor explaining high sympathetic nerve activity in women with PCOS (Sverrisdottir et al., 2008).

Recently it was demonstrated that repeated low-frequency EA and physical exercise lowers high sympathetic nerve activity in women with PCOS. Thus, treatment with low-frequency EA

or physical exercise to reduce sympathetic nervous activity may be of importance for women with PCOS (Stener-Victorin et al., 2009).

Support for this observation can be found in experimental animal research. In an oestradiol valerate (EV)-induced rat PCO model, transection of the superior ovarian nerve reduces the steroid response, increases  $\beta_2$ -adrenoceptor expression to more normal levels, and restores oestrus cyclicity and ovulation (Barria et al., 1993). Also, blockade of endogenous NGF action restores the EV-induced changes in ovarian morphology and expression of the sympathetic markers  $\alpha_1$ - and  $\beta_2$ -adrenoceptors, the p75 neurotrophin receptor, NGF-tyrosine kinase receptor A and tyrosine hydroxylase. These data confirm the close interaction between NGF and the sympathetic nervous system in the pathogenesis of steroid-induced PCO in rats (Manni et al., 2005b). In line with these observations, repeated low-frequency EA reduces high ovarian concentrations of NGF (Stener-Victorin et al., 2000, 2003b), CRF (Stener-Victorin et al., 2001) and endothelin-1 (Stener-Victorin et al., 2003b) in EV-induced PCO. It also modulates hypothalamic  $\beta$ -endorphin concentrations and immune function (Stener-Victorin and Lindholm, 2004) in the same rat PCO model.

To investigate the hypothesis that repeated low-frequency EA treatments and physical exercise modulate sympathetic nerve activity in rats with EV-induced PCO, we studied the expression of mRNA and protein of the  $\alpha_{1a}$ -,  $\alpha_{1b}$ -,  $\alpha_{1d}$ - and  $\beta_2$ -adrenoceptors, the p75 neurotrophin receptor, and tyrosine hydroxylase. Four weeks of physical exercise almost normalised ovarian morphology (Manni et al., 2005a), and both EA and exercise normalised the expression of NGF, NGF receptors, and  $\alpha_1$ - and  $\alpha_2$ -adrenoceptors (Manni et al., 2005a,b).

Further, in rats with DHT-induced PCOS exhibiting reproductive and metabolic abnormalities, both low-frequency EA and exercise improved ovarian morphology, as reflected by a higher proportion of healthy antral follicles and a thinner theca interna cell layer than in untreated PCOS (Manneras et al., 2009). This was accompanied by improved oestrus cyclicity.

Low-frequency EA also increased ovarian blood flow. The needles were placed in the abdominal and hind limb muscles, which have the same somatic innervation as the ovaries and uterus (Stener-Victorin et al., 2003a, 2004, 2006). The response was mediated by ovarian sympathetic nerves as a reflex response controlled by supraspinal pathways (i.e. CNS) (Stener-Victorin et al., 2003a, 2006). Interestingly, electrical stimulation of the superior ovarian nerve affected the ovarian blood flow response and reduced ovarian oestradiol secretion rate, an effect that was mediated via  $\alpha$ -adrenoceptors in the regulation of ovarian function by electrical stimulation (Kagitani et al., 2011), ovarian function.

These findings support the theory that increased sympathetic activity contributes to the development and maintenance of PCOS and that the effects of EA and exercise are mediated by modulation of sympathetic outflow to the adipose tissue and ovaries. Augmented sympathetic activity in PCOS may contribute to vascular risk factors associated with the condition. Thus, therapies aimed at reducing sympathetic activity in PCOS need to be studied.

## URINARY BLADDER

The urinary bladder and sphincters are innervated by sympathetic, parasympathetic and somatic nervous systems (Kim et al., 2010; Thor and Donatucci, 2004). The ANS has an important role in the regulation of urinary bladder function. Consequently autonomic dysfunction may disrupt bladder function and sphincter activity and most likely contribute to pathogenesis of overactive bladder and urge incontinence (Kim et al., 2010; Thor and Donatucci, 2004) and lower urinary tract symptoms (Im et al., 2010). This mechanism has also been demonstrated by the fact that women with overactive bladder demonstrate predominantly a sympathetic overactivity (Hubeaux et al., 2007, 2011).

In experimental studies it has been demonstrated that acupuncture-like stimulation of perineal muscles inhibits contraction of the urinary bladder, thus allowing bladder filling (Sato et al., 1992,

1997). These experimental observations are supported by clinical findings where acupuncture treatment has been shown to improve bladder capacity, urgency and frequency in women with urgency incontinence (Bergstrom et al., 2000; Emmons and Otto, 2005). For more details see Chapter 27.

## GASTROINTESTINAL TRACT

The gastrointestinal (GI) tract is innervated by intrinsic neurons of the enteric nervous system and by the axons of extrinsic sympathetic, parasympathetic and visceral afferent neurons (Phillips and Powley, 2007). The sympathetic innervation originates from the prevertebral sympathetic ganglia and its noradrenergic fibres project to the wall of the GI tract (see Table 6.1). The vagal (parasympathetic) nerve supplies both sensory (afferent fibre) and motor (efferent fibre) functions.

The group of Professor Sato has systematically elucidated how acupuncture-like stimulation modulates visceral reflexes. Manual acupuncture stimulation of abdominal and lower chest muscles almost always inhibits gastric motility, while the stimulation of limbs facilitated gastric motility in approximately two-thirds of the anaesthetised rats tested (Sato et al., 1993). This inhibitory response in gastric motility remained after bilateral severance of the vagal nerves but was abolished after severing the sympathetic nerve branches to the stomach. Thus, the inhibitory response is due to activation of spinal reflexes. The inhibitory response remained after spinal transection, indicating that the spinal cord is essential for the response (Sato et al., 1993). These experimental data indicate that acupuncture may have a therapeutic effect on bowel disease, e.g. irritable bowel syndrome (IBS).

The pathogenesis of IBS remains unknown. Up-regulation of neural processing between the gut and the brain (brain-gut axis) resulting in alterations in gut motility, secretion and visceral sensation has been proposed (Mazur et al., 2012). Importantly, the ANS mediates brain-gut interactions and dysfunction in the ANS, and so may, at least in part, be responsible for IBS (Mazur et al., 2007, 2012). Interestingly, acupuncture for IBS has been shown to provide an additional benefit over usual care alone with a long-lasting effect (MacPherson et al., 2012). Commonly used points were CV4, CV10, CV12, ST25, LR3, SP4 and SP6 all located in the innervation area of the gut. For more details see Chapter 21.

## SALIVARY AND LACHRYMAL GLANDS

There is a close relation between salivary and lachrymal gland function and autonomic regulation. The major salivary glands include parotid, submandibular and sublingual glands with the major physiological function to secrete saliva, which is essential for the lubrication, digestion, immunity and overall maintenance of homeostasis within the body (Ferreira and Hoffman, 2013). Saliva secretion is mediated by both parasympathetic and sympathetic autonomic innervation (Ferreira and Hoffman, 2013).

The parasympathetic innervation involves cranial nerves VII and IX, and the sympathetic innervation is formed by the cervical sympathetic nerves via the medial basal hypothalamus-pituitary complex. Neurotransmitters for parasympathetic fibres are the classical acetylcholine together with VIP and CGRP, which increase both salivary gland blood flow and salivary secretion (Ekstrom et al., 2013; Ferreira and Hoffman, 2013). Major sympathetic neurotransmitters are the classical NE together with SP and NPY, which inhibits blood flow and cause vasoconstriction.

A common clinical condition affecting salivary glands is Sjögren's syndrome, a systemic autoimmune disorder affecting salivary gland function. The aetiology of Sjögren's syndrome is not known but the involvement of nerves causing the damage has been suggested, leading to a secondary inflammatory response. Another major clinical cause of salivary hypofunction (xerostomia) is injury after radiotherapy for head and neck cancer. Xerostomia postradiotherapy can be permanent and is multifactorial, involving damage to salivary gland epithelial cells, the blood vessels and the associated nerves (Ferreira and Hoffman, 2013).

In patients with Sjögren's syndrome, acupuncture with manual or low-frequency (2 Hz) electrical stimulation has been demonstrated to increase local blood flux as measured by laser Doppler flowmetry (Blom et al., 1993a,b). A possible mechanism of action of the increased salivary flow rates may be that acupuncture increases the secretion and release of the neuropeptides VIP and CGRP (Dawidson et al., 1998, 1999).

The xerostomia caused by irradiation therapy has also been demonstrated to be improved by acupuncture. Acupuncture given concurrently with radiotherapy reduced xerostomia as demonstrated by increased salivary flow and improved quality of life (Meng et al., 2012). Eight sessions of weekly group acupuncture compared with oral care education reduced most symptoms including need to drink during the night, and improved swallowing function in patients suffering from chronic radiation-induced xerostomia (Simcock et al., 2013). Common needle placement was in LI2, LI20, local points located over the glands and auricular points. Both manual stimulation and low-frequency electrical stimulation has been applied.

Experimental and clinical findings provide evidence that acupuncture relieves xerostomia in patients with both Sjögren's syndrome and xerostomia due to irradiation therapy. The effect is most likely mediated via modulation of autonomic control of the salivary glands.

## Concluding comments

Increasing evidence demonstrates that the effect of acupuncture on visceral, endocrine and metabolic function to large extent is mediated via modulation of autonomic reflexes at spinal and central level. It is of importance to study the effect of acupuncture stimulation (manual and/or electrical) in different organ systems as it may evoke different effects. Experimental studies also demonstrates that the effect differs depending on where needles are placed and how they are stimulated.

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## *Clinical approaches*

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# Western medical acupuncture – the approach to treatment

M. Cummings

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## Introduction

This chapter describes the theoretical approach to the use of acupuncture that has become known as Western medical acupuncture (White, 2009). It is based on the results and interpretation of experimental data into neurophysiological mechanisms of sensory stimulation combined with aspects of the historical record of acupuncture from East Asia (mainly China).

It is assumed that the reader has prior knowledge of common needling techniques as these are not described here – please refer to the related textbook *An Introduction to Western Medical Acupuncture* (White et al., 2008b).

The chapter starts with a description of the principles used in point selection from the neurophysiological perspective and then goes through each aspect of the principles including local needling, segmental approaches and the relevant features of needling anywhere in the body for general effects. The chapter is completed with a discussion of the other potential effects related to treatment other than the direct physiologic stimulus of needling. The latter are referred to as context effects, and some are relevant to the effects observed in sham or placebo groups in randomised controlled trials (RCTs).

## Principles of point selection

This section provides a summary of the approaches to choosing sites for needling that are used in Western medical acupuncture (WMA) to treat a condition that affects a local part of the body, typically pain, which may be direct or indirect approaches; followed by other indirect approaches to treatment of more general conditions. Many topics will be covered in more detail later in the chapter.

### DIRECT APPROACHES

#### Local

Local acupuncture needling is used to treat somatic conditions, often peripheral sources of musculoskeletal pain. Typically needling is applied directly into the problem area or within a couple of centimetres, and may produce effects in different ways. This approach involves direct needling effects on muscle, either via mechanical effects on trigger points (see the next section) or reflex inhibition of muscle tone (Graven-Nielsen et al., 2008; Mense and Gerwin, 2010; Mense et al., 2001; Simons and Mense, 1998). Local needling also potentially affects tissues via antidromic stimulation of small diameter sensory nerves that mediate trophic effects via release of vasoactive neuropeptides and growth factors (see Chapter 3 for more detail). This local needling will also have the potential to incur segmental effects, as described in the following paragraph.

Local points are typically categorised as trigger points, tender points (TePs) or (classical) acupuncture points. Some practitioners would add a category for anatomical points chosen by tissue and proximity, i.e. needling anywhere in an area of muscle or onto an area of periosteum.

#### Segmental (dorsal and ventral)

Segmental effects are mediated via the dorsal (sensory) horn of the spinal cord at the level stimulated. Some effects may be brought about by direct connections in the dorsal horn, but most are thought to be mediated via long connections to and from the brainstem. These effects may be stimulated by needling very close to a problem in the soma (local needling) or by stimulating any deep somatic nerves in the distribution of the same or even contralateral spinal nerve. Superficial nerves to skin may mediate effects as well, but these effects may be more akin to transcutaneous electrical nerve stimulation (TENS) in humans – see Chapter 15. This applies to both ventral and dorsal rami, but the effects may vary in magnitude, and it is thought that pain or dysfunction derived from ventral structures is probably best treated by targeting ventral segments and vice versa.

### INDIRECT APPROACHES

#### Perisegmental

This approach is specifically used in the case of neuropathic pain conditions, when direct needling would be too uncomfortable and may exacerbate the condition. Points are chosen in segments close to the affected segment, typically above and below, but also the contralateral segment may be used (White et al., 2008b).

#### Distant non-segmental and general (for central or non-localised conditions)

The influence of acupuncture from needles that are not in or close to a segmental region is via general effects in the brain and throughout the spinal cord. These effects tend to be less powerful than the direct effects, and therefore the treatment intensity or total dose (of needles) chosen

is often greater under these circumstances, unless the approach is used simply to augment local and segmental approaches. The precise location of needling to mediate these effects is unlikely to be important, although there may be regional differences (discussed in the succeeding text), and points in the limb muscles may be more potent than those on the trunk.

## Microsystems

There are many systems within the field of acupuncture where a localised and accessible anatomical area is used in an attempt to influence distant sites. Perhaps the most well known are the ears and scalp. Ear acupuncture was the first to be described. Its origin is attributed to a French physician called Nogier (Nogier, 1972), who postulated that the ear looked rather like a curled up foetus with the head at the lobe of the ear and the spine around the antihelix. Hence a somatotopic map of the body was imagined on the ear and facilitated a system where conditions could be treated by needling the ear alone. A similar system was developed in the scalp by Yamamoto (White et al., 2008b). Neither system has convincing evidence to support the somatotopic maps, however, there is reasonable clinical evidence to support the effectiveness of needling the ear (see Chapter 10) and the scalp, particularly in pain conditions (Asher et al., 2010; Usichenko et al., 2008) but also for situational anxiety in the case of ear acupuncture (Pilkington et al., 2007).

## Myofascial trigger points

### THE CLINICAL PHENOMENON AND TERMINOLOGY

Myofascial trigger points (MTTrPs) are exquisitely tender regions in the mid-fibre portion of palpable taut bands of skeletal muscle (Travell and Rinzler, 1952; Travell and Simons, 1983). They are referred to as points because their size appears to be smaller than the dimensions of the examiners palpating fingertip. Hence a single 'point' of maximal tenderness can be found. When a fine filiform needle is used as the examining probe, the findings appear to be different. There is no longer a single point of maximal mechanical sensitivity, but multiple points within the area as determined by local motor responses (the local twitch response or LTR in the taut band) and needle electromyographic activity.

Pressure applied to MTTrPs (also referred to in the shorter form as trigger point - TrP) can elicit local pain and referred pain that is characteristic for individual skeletal muscles (characteristic referral pattern of pain) (Simons et al., 1999). In the case of a symptomatic individual with myofascial pain, the pain caused by pressure may be recognised as being the pain of which the individual is complaining (recognition of pain). Snapping palpation across the fibres of an active (symptomatic) TrP often results in an apparently involuntary withdrawal of the body away from the palpating finger. This is called the jump sign. LTRs are also seen in this form of cross-fibre palpation, but most practitioners find these difficult to elicit (Gerwin et al., 1997). LTRs are more easily elicited by needling with a fast insertion into the TrP (Hong, 1999). It is interesting to note that this style of needling appears to elicit LTRs from a rather discrete area of the taut band, and that a location as little as 5 mm away may elicit no LTRs. Occasionally LTRs are seen on insertion through the fascial outer layer of the muscle, and this phenomenon probably equates to what electrophysiologists refer to as 'insertional activity' (Chu and Schwartz, 2002). The physiological corollary is likely to be a localised stretch reflex from distortion and sudden release (on penetration of the needle tip) of the superficial muscle fibres. This is likely to be different from the LTRs that are associated with taut bands and pain recognition by the individual.

Muscles with active TrPs, i.e. those causing spontaneous pain, are invariably associated with reduced range of motion in the associated joint or joints, and needling of the TrPs often restores the range of motion immediately. The occurrence of LTRs during needling appears to correlate with a more complete response (Hong, 1994) and restoration of range, although this is a clinical impression and inevitably subject to observer bias (Box 7.1).

**BOX 7.1 ■ The clinical characteristics of myofascial trigger points**

Tender point (small tender region)  
 Taut band (often palpable)  
 Characteristic pattern of pain  
 Jump sign with pain recognition  
 Local twitch response

MTrPs can be found in the postural skeletal muscles of the majority of adults (Cummings and Baldry, 2007; Sola et al., 1955), almost as if they represent a normal ageing phenomenon of skeletal muscle. In the absence of a clinical pain complaint, or spontaneous pain (i.e. pain experienced without external pressure), these are referred to as latent. In patients presenting with pain, whose pain can be reproduced with digital pressure over an MTrP or pressure applied via a needle tip within muscle, these MTrPs are referred to as active. MTrPs frequently appear to be the primary source of musculoskeletal pain in young to middle-aged adults (primary myofascial pain, or primary MTrPs), and local treatment to the active MTrP, such as with stretch or pressure (via hands or a needle) or both, often appears to be immediately effective (Cummings, 1996). There is little clinical research to support this observation, probably because of the difficulty of recruiting the ideal population within the framework of the RCT. It is easier to recruit patients with more chronic persistent regional pain conditions, who are likely to have other sources of musculoskeletal pain as well as MTrPs. For example, early cervical spondylosis and osteoarthritis is frequently associated with muscle pain (particularly in trapezius), and it can be difficult to determine to what degree these conditions coexist or are interdependent. In many cases, the MTrPs are considered secondary to the changes in the axial skeleton (secondary myofascial pain, or secondary MTrPs), however, since the latter are likely to occur anyway with age, it is possible that the MTrPs are not always directly related. Having said that, it is a frequent observation that symptomatic MTrPs occur in the region of another pain source, whether that be somatic (e.g. osteoarthritis) or visceral pain. These secondary MTrPs may also occur in an area of referred pain, in this case they are called satellite trigger points (satellite MTrPs being a subset of secondary MTrPs).

**Clinical points**

MTrPs may be the primary cause of pain, or secondary to other painful conditions.

**Clinical points**

Experience suggests active MTrPs that are primary respond quickly to needling.

**Trigger points in other tissues**

In the original Trigger Point Manual by Travell and Simons (Travell and Simons, 1983, 1992), the MTrPs I have described earlier were referred to as central MTrPs, i.e. they were found in a central zone of the muscle fibres, which might be consistent with the endplate zone (Simons et al., 2002). Trigger points were also described in almost all other somatic tissues, including skin, fascia, tendon, ligament and periosteum. In these cases the trigger point is defined by its discrete location at the point of the palpating fingertip and the triggering of a recognised pain complaint. So these are potential peripheral pain generators that are identified by the fingertip in conditions such as tendinopathy. It is better to refer to these as TePs that reproduce familiar pain and reserve the term trigger point for the central MTrP phenomenon within the endplate zone of contractile skeletal muscle.

## Therapeutic needling

Needling of MTrPs appears to be highly effective, and the techniques are very popular within physical medicine, although clinical research is limited (Cummings and White, 2001; Kietrys et al., 2013; Tough et al., 2009). Needling appears to be more effective when pain recognition and an LTR is elicited, and in the uncomplicated cases of isolated primary MTrPs, a single needle insertion may be all that is required.

## THE MECHANISTIC BASIS OF THE PHENOMENON

Various theories have been put forward for the cause of discrete soft tissue pain over the last two centuries or so, and a very comprehensive narrative review of these can be found in the Trigger Point Manual by Travell and Simons (Simons et al., 1999). The leading contemporary theory focuses on motor endplate dysfunction and a localised energy crisis in surrounding sarcomeres (the contractile units of skeletal muscle) (Simons, 2008). An alternative theory prefers to centre on the muscle spindle (Partanen, 1999; Partanen et al., 2010), but this does not seem to explain all the clinical phenomena as convincingly as the former theory.

### Motor phenomenon

First we should explain the palpable taut band since this seems ubiquitous in adult skeletal muscle, and is therefore likely to be a precursor to the active MTrP. The taut band has both motor and sensory features. It is palpably harder than surrounding muscle tissue, although this can change during palpation or treatment so that it may become less easy to feel or even disappear entirely. This would suggest that it is formed from contraction (i.e. modifiable tension) rather than contracture (i.e. permanent shortening) (Graven-Nielsen et al., 1997, 2008; Mense and Gerwin, 2010; Mense et al., 2001; Simons and Mense, 1998), although chronic MTrPs do appear to be hard and persistently palpable. Often the most tender or active MTrPs are not in these chronic hard bands, but in the slightly more compliant bands in the same vicinity. Histologically, no structure has been identified to explain these chronic solid bands in muscle, and they appear similar to normal muscle tissue on cross-section in biopsy studies, but it is tempting to consider that they are at a late stage of the pathophysiological process of MTrPs. Since palpable bands can sometimes disappear with physical treatments, it is perhaps understandable that they also disappear on muscle biopsy, since the muscle is no longer physiologically active. However, some studies have described abnormal histological findings (De Stefano et al., 2000; Glogowski and Wallraff, 1951; Miehlike et al., 1960; Reiting et al., 1996; Simons, 1999; Simons and Stolov, 1976).

### Clinical points

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Palpable taut bands in muscle are due to sustained mid-fibre contraction – not contracture and not ‘muscle spasm’.

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While on the subject of physiological or pathophysiological motor activity within taut bands, there are two more motor phenomena that we need to be able to explain within our theoretical model. First is the LTR (Simons et al., 1999; Travell, 1955a,b; Weeks and Travell, 1955). This is a contraction within the taut band that occurs with a sudden mechanical load applied by snapping palpation across the MTrP, fast needle insertion into the MTrP or a blunt impact in an experimental setting. An experimental study by Hong et al. suggests that the LTR has a latency that equates to that of a spinal reflex following the mechanical impact (Hong et al., 1995). This might be seen to favour the muscle spindle as the key substrate of the MTrP, however, another possibility (the author's theory) is that the mechanical insult to dysfunctional endplates may result in an imperceptible contraction of just a few muscle fibres that go on to stimulate a single muscle spindle and initiate a spinal reflex contraction of the related motor unit or units, which would be visible.

The second phenomenon is visible regional contraction of muscle tissue within the central zone of muscle fibres at an MTrP. This has been observed by the author immediately following pincer grip snapping palpation of the upper free border of trapezius in several very slim individuals with active MTrPs. It represents contraction of central sarcomeres and lengthening of others in the same muscle fibres. This phenomenon is unusual and distinct from the usual coordinated contractions of sarcomeres that occurs following motor nerve, endplate and consequent muscle cell depolarisation. One possible explanation is that the mechanical stimulus to the trigger point (probably at the endplate zone) results in local release of calcium ions from the sarcoplasmic reticulum. This may be due to a pathophysiological change in the vicinity of dysfunctional endplates where the membrane potential is chronically unstable – possibly leaky ryanodine channels (RyR1) in sarcoplasmic reticulum (Andersson et al., 2011).

### Electromyography

Naturally MTrPs, as a pathophysiological condition of skeletal muscle tissue, have been extensively investigated with electromyography for many years. Surface electrodes do not appear to pick up local specific abnormalities at MTrPs, but can measure more generalised characteristics of affected muscles, such as increased responsiveness, accelerated fatigability, delayed recovery and delayed relaxation (Simons et al., 1999). Needle electrodes, and in particular coaxial needle electrodes, can detect abnormal electrical activity at MTrPs. In 1957 Weeks and Travell described high frequency spike discharges from MTrPs compared with electrically silent adjacent muscle (Simons et al., 1999). In 1993, Hubbard and Berkoff reported similar electrical activity as being characteristic of MTrPs (Hubbard and Berkoff, 1993). Subsequently Simons, Hong and Simons investigated the phenomenon using increased amplification and sweep speed and noted two components to the electrical activity: spike waves and a noise-like component that they referred to as spontaneous electrical activity (SEA) (Simons et al., 1999). However, this activity was very similar to the normal motor endplate potentials (EPPs) described by electromyographers (Wiederholt, 1970). More focused study seems to suggest that SEA observed at MTrPs is an exaggerated form of normal EPPs (Simons et al., 2002). Whether or not the SEA at MTrPs is considered abnormal EPPs or normal EPPs, either way this seems to add weight to the theory that motor endplates are a key feature of the clinical entity that is an MTrP.

### Clinical points

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Spontaneous electrical activity at MTrPs is probably from endplate potentials.

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### Sensory phenomena

MTrPs are tender – they have a lower pressure pain threshold (PPT) than surrounding muscle. The central, most active (i.e. where motor activity, such as the LTR, is most easily initiated) portion of a taut band is more sensitive to pressure than the rest of the band, and the band is more sensitive than surrounding normal muscle (Hong et al., 1996). It should be noted that muscle tissue is generally more tender (has a lower PPT) than other soft tissues, it is metabolically very active and has a rich sensory nerve supply (Mense et al., 2001). Mechanical pressure on muscle creates a dull aching pain in the local area, and if the mechanical pressure is maintained the pain increases and spreads in a typical referral pattern that appears to be characteristic to some degree for each skeletal muscle. This referred pain pattern is most easy to elicit from active MTrPs (Hong et al., 1997), but can also be elicited from latent MTrPs and indeed from normal muscle. The referred pain phenomenon is due to central nervous system (CNS) integration of incoming sensations (Graven-Nielsen and Arendt-Nielsen, 2008; Mense and Gerwin, 2010; Mense et al., 2001; Simons and Mense, 1998), and not necessarily a special attribute of muscle. So in a sense the motor and sensory features of MTrPs are distinct and can therefore vary in individuals. Increased metabolic activity and compromised circulation in taut bands can create a milieu that

will sensitise sensory nerve endings. However, the degree to which these sensitised nerve endings result in perception of pain and suffering of the animal will also depend on the tendency of the CNS to amplify or inhibit the incoming sensations. So some individuals may have prominent taut bands and restriction of joint range without perceiving great pain, and others may have minimal functional restriction or palpable abnormality and yet perceive severe pain.

## THE NEEDLE EFFECT

Needling has several potentially useful functions in the assessment and treatment of myofascial pain. Filiform acupuncture needles have a fairly uniform smooth curved surface to the tip, and do not have the cutting edge of standard hypodermic needles for injection. On insertion they exert a mechanical load by applying pressure at the tip and cause some tissue distortion due to resistance of tissue against the moving needle shaft – resistance to movement is most noticeable on withdrawal of a needle that is deeply inserted into a muscle layer, but it can also occur on insertion or withdrawal at the skin level. Pressure at the tip increases when there is resistance to penetration at skin, fascial layers and on reaching a firm endpoint (enthesis, periosteum and tendon). Tissue distortion at the needle tip is reduced in soft tissue layers (skin, fascia and muscle) by increased speed of penetration, and this means that in general, faster insertion through skin and fascial layers is less painful (Yin et al., 2011). Resistance to penetration varies depending on the nature and state of the tissue, the gauge of the needle and the shape of the needle tip. With good quality fine needles (say 0.25–0.30 mm diameter) it is possible to tell the difference between subcutaneous fat, muscle, enthesis (or ligament) and periosteum by the degree of resistance. This is useful when assessing pain since the needle can act like an extension to the examiner's finger and often helps determine the precise tissue that is the source of a peripheral pain.

Pressure applied by the needle is one thing, but another important factor is the mechanical sensitivity within tissues. The latter can vary considerably in both normal subjects and in patients with pain conditions. There appears to be relatively consistent increased sensitivity to needle tip pressure in the walls of blood vessels, and the nature of the sensation produced is unpleasant. Needle penetration of fascial layers tends to create heightened sensation, but it is not clear whether this is due to increased pressure sensitivity of the tissue or to the increased mechanical loading due to its higher resistance (than muscle and fat tissue) to penetration with the needle tip. Muscle of normal tone seems to have uniform resistance and sensation, or lack thereof. Sensation and resistance to penetration increase with increasing muscle tone, and it seems logical to assume that this relates to increased pressure applied at the needle tip. MTrPs appear to be highly sensitive to needle penetration, and while they have a degree of increased tone within the taut band, the latter is not usually detectable on needle penetration, so the exquisite sensitivity must be related to increased sensitivity of the tissues. This increased sensitivity has been documented through measuring PPTs as noted earlier, however, the sensitivity on needle penetration appears to be in multiple very small loci within the 'TeP' (of the taut band) that is found with the examiners fingertip.

### Clinical points

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MTrPs are highly sensitive to needling.

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Fast insertion of a needle into an MTrP causes both heightened sensation (and often pain recognition in a patient) and an apparently simultaneous LTR. Fast insertion seems to produce LTRs more often than slow insertion, and this may be due to higher mechanical loading at the MTrP or a reduced potential for the taut band and MTrP to move away from the needle trajectory, or a combination of both of these factors.

### Clinical points

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A LTR is likely when a needle is rapidly inserted into the MTrP.

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The observed therapeutic effect of acupuncture or dry needling in myofascial pain requires explanation, possibly with a number of mechanisms since a variety of different techniques have been associated with positive effects. Evidence for efficacy is rather limited, so this is all rather speculative. Needling techniques can be divided into direct and indirect techniques, where direct techniques target the location of the trigger point and indirect ones do not.

### Direct needling techniques

Direct needling of trigger points may be in a gentle, acupuncture-like style where LTRs are not elicited, or more vigorous with repeated fast insertion to elicit LTRs (Hong and Simons, 1998). The latter is generally referred to as dry needling. Gentle direct needling without LTR may elicit spinal modulation of pain or reduced muscle tone or both. The local effect of needling may also result in improved blood flow and hence oxygenation of tissues (Sandberg et al., 2003, 2004, 2005). Since relative hypoxia and low pH is a feature of chronic myalgia, a temporary improvement in blood flow may normalise this adverse environment and thus reduce the sensitisation of local nerve endings. Fast insertion with LTR may exert similar effects (Hong and Simons, 1998; Hong, 1994), but in addition, the fast insertion may directly damage endplates or muscle fibres, which then take some time to repair and reinnervate.

### Clinical points

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Acupuncture's effect on MTrP is probably due to trauma to endplates, increased local blood flow and spinal modulation of pain.

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### Indirect needling techniques

Indirect techniques can be local or at a distance from the trigger point. Indirect techniques are likely to exert their effects through spinal neuromodulation, with local techniques utilising segmental sensory modulation and distant techniques utilising mechanisms more akin to heterotopic noxious stimulation (Sprenger et al., 2011) (formerly known as diffuse noxious inhibitory controls).

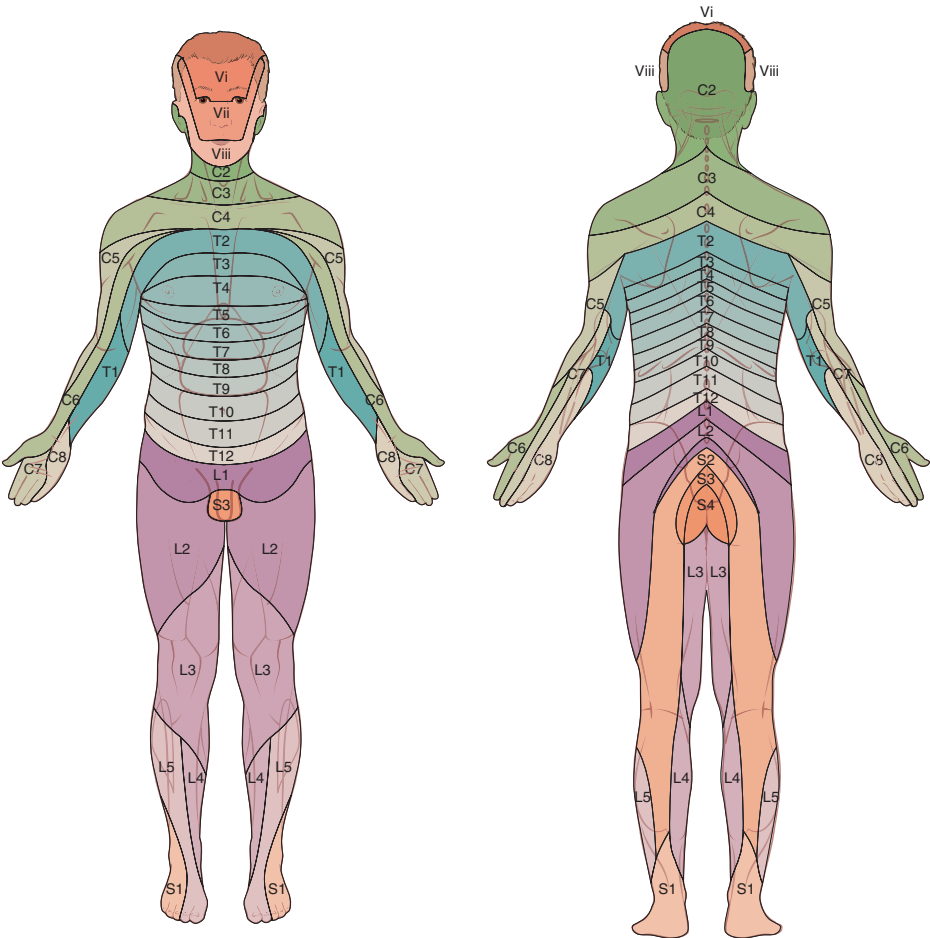
## Segmental acupuncture

### DEFINITION AND INTRODUCTION

Segmental acupuncture refers to needling of any region of the soma that is innervated by the same spinal nerve as the 'target' tissue (Filshie and Cummings, 1999), i.e. the tissue or organ responsible for the patient's complaint. Most spinal segments are associated with a dermatome (an area of skin), myotome (a region of muscle), sclerotome (an area of periosteum) and viscerotome (a region of viscera) based on their common innervation from the same segment of spinal cord. The segmental approach is only necessary if the target tissue cannot be needled directly. This is most relevant when treating visceral conditions, but peripheral neuropathic complaints in the soma may also need to be approached in this way because direct needling of the region may be too painful (White et al., 2008b).

### EMBRYOLOGY – SEGMENTATION

Some knowledge of the segmental arrangement of the soma and viscera is required to determine the best sites for needling. Segmentation begins around day 19–21 (stage 9) in the human embryo (Müller and O'Rahilly, 2003), and the neat ordered arrangement of the somites is later distorted by limb bud formation and their subsequent growth, and by some differential growth on the dorsal and ventral sides of the spine. I like to use the example of a simple earthworm, which is a neatly segmented creature with a hole at each end and no limbs. The segments occur in sequence from the hole at the front (the mouth) to the hole at the end (the anus). The human embryo resembles



**Figure 7.1** Dermatome map based on information derived from Gray's Anatomy.

a rather flat worm for a short while, before the segmental simplicity is ruined by the hole at the front moving (as a degree of flexion of the embryo occurs), and the limb buds forming and dragging their ventral segments to form the limbs. The final arrangement can most easily be viewed by looking at a dermatome map (Fig. 7.1).

## THE PRACTICAL APPROACH

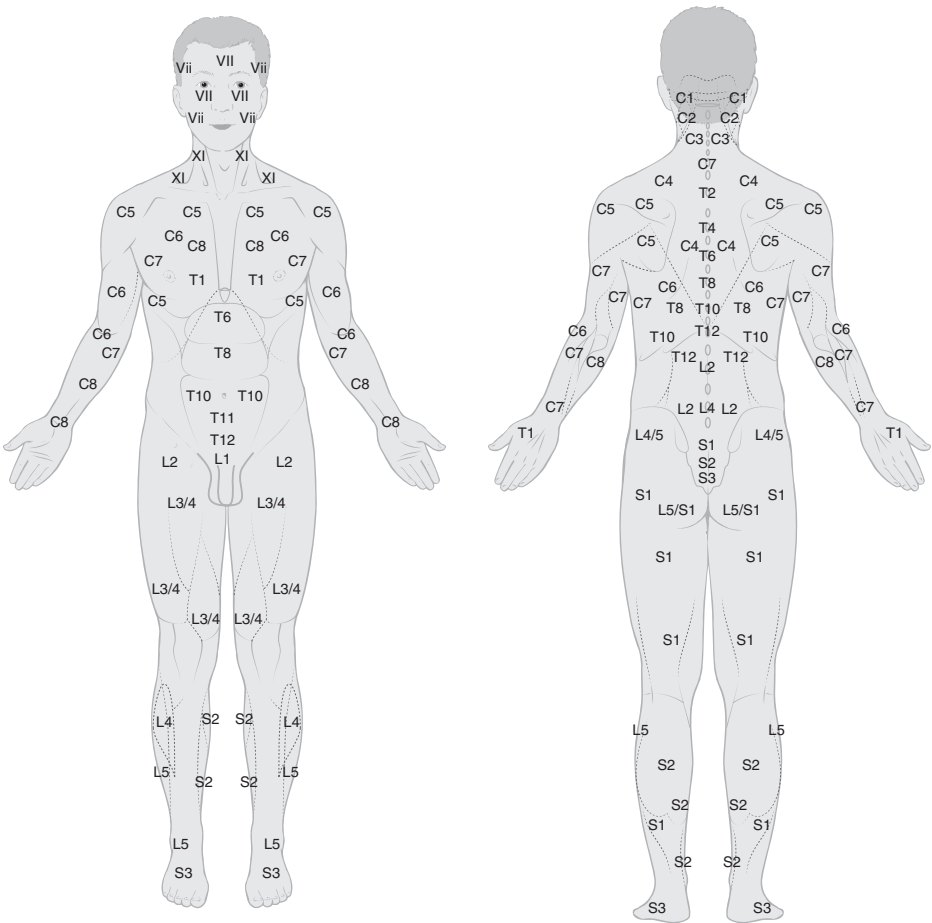
Acupuncture mostly aims to stimulate nerves in deep somatic tissue, so we are most interested in the segmental innervation of muscle, or the myotomes. Dermatomes are traversed with the needle but stimulation of skin has only temporary effects, so we are not interested in these segments unless we chose to use indwelling needles or constant stimulation with an electrical stimulator (TENS). Occasionally we target periosteum, but the segmental innervation of periosteum (sclerotome) is not as precisely known as that of skin or muscle because damage of nerves to skin or muscle results in functional losses that can be objectively assessed in terms of skin sensation or muscle weakness. The same is not true of periosteum. Figure 7.2 illustrates the segmental muscle innervation in the common regions that may be needed for segmental purposes. Note that in

some areas, particularly the low back, the segmental innervation of skin (see [Fig. 7.1](#)) can be quite different from that of the muscle beneath.

### Clinical points

Acupuncture generally acts through nerves in muscles, so myotomes are most relevant when using segmental acupuncture.

Having assessed a patient and determined the likely source of symptoms, the practitioner needs to first consider the segmental levels into which the relevant neural activity is transmitted. If it is a visceral complaint, then a list of autonomic innervation of the organs is useful ([Table 7.1](#)). The dorsal horns where neural activity is most prominent can then be stimulated via somatic nerves in the hope of modulating pain or autonomic efferent activity or both. Often we need to consider several segments, and be aware that our needles will each stimulate a range of segments, so absolute accuracy is not necessary, we only require to be in the correct segmental region (a range of perhaps 3–5 segments).



**Figure 7.2** Myotome map for acupuncturists – this diagram illustrates the likely myotome target from needling into muscle tissue in the areas indicated by the segmental nomenclature. Derived from information included in Gray's Anatomy.

**TABLE 7.1 ■ Viscerotomes – the autonomic innervation of the viscera, plus the sympathetic innervation of the soma based on data derived from Gray's Anatomy (Gray et al., 1995; Standing, 2005)**

Viscus or viscera	Sympathetic	Parasympathetic
Heart	T1–T5	Vagus
Bronchi and lung	T2–T4	Vagus
Oesophagus (caudal part)	T5–T6	Vagus
Stomach	T6–T10	Vagus
Small intestine	T9–T10	Vagus
Large intestine to splenic flexure	T11–L1	Vagus
Splenic flexure to rectum	L1–L2	S2–S4
Liver and gallbladder	T7–T9	Vagus
Spleen and pancreas	T6–T10	Vagus
Kidney	T10–L1	Vagus
Ureter	T11–L2	Vagus
Suprarenal	T8–L1	Vagus
Testis and ovary	T10–T11	Possibly vagus
Urinary bladder	T11–L2	S2–S4
Prostate	T11–L1	S2–S4
Uterus	T12–L1	S2–S4
Fallopian tube	T10–L1	S2–S4
<i>Soma</i>		
Head and neck	T1–T5	Four cranial nerves/nil to soma
Upper limb	T2–T9	Nil
Lower limb	T10–L2	Nil

### Common somatic pain complaints

Segmental considerations are rarely used in common musculoskeletal pain complaints since local and regional points will be in the appropriate segment. Some clinical experts, particularly in the field of dry needling or myofascial pain, promote the addition of needling dorsal segmental paraspinal muscle (multifidus) at the level related to the problem (see the discussion of the innervation of multifidus in the succeeding text). While this approach may have theoretical benefits, there is no objective data to support it as yet. Local needling of musculoskeletal pain sources has the potential advantage of both promoting local healing responses, and blocking nociceptive transmission, as well as creating a conditioning stimulus that mediates segmental spinal pain and autonomic modulation.

### Neuropathic pain from the soma

Nerve damage results in neuropathic pain in a small proportion of cases (perhaps 5–10%). This is often associated with increased skin sensitivity (allodynia, hyperaesthesia) in discrete regions related to the innervation territory of the nerve. In this case, local needling in the area of pain would often be too uncomfortable for the patient. The most common approach used in this situation is referred to as a perisegmental approach (White et al., 2008b). This refers to needling segments above and below, and perhaps on the contralateral side of the body (mirror points). In these areas the tissue is of normal sensitivity, and needling will stimulate descending spinal segmental modulation that will cover the pathological segments too. This appears to be the best and most easily tolerated approach. In some circumstances it is possible to needle into dysaesthetic areas, but totally anaesthetic areas are avoided because there can be no benefit in terms of nerve stimulation.

## Visceral conditions

The viscera are not generally accessible to local treatment, except perhaps intraoperatively, and the basis for this is questionable (Xin et al., 2002). So the approach to visceral conditions has to be indirect, whereas by contrast the local treatment of musculoskeletal pain is direct and segmental. Indirect treatment can be segmental or non-segmental. Here I will deal with the indirect segmental approach to visceral conditions.

Following appropriate diagnosis of the condition, using ‘overactive bladder’ as an example, you need to recall (or look up) the segmental innervation of the organ involved, or more specifically, determine the spinal segmental levels at which the sensory and autonomic nerve activity is most active related to the condition under treatment, as listed in [Table 7.1](#). It is at these levels that the conditioning stimulus created with acupuncture should be targeted. The choice of areas for stimulation is based on the appropriate level of somatic innervation, knowledge of anatomy and the comfort and convenience for the patient.

Each somatic segment can be divided into dorsal and ventral parts based on the distribution of the primary rami i.e. the first division of the spinal nerves into the dorsal and ventral primary rami. Since the viscera are ventral structures, their sensory network in the dorsal horn is likely to be more closely related to that of the ventral soma (i.e. skin and muscle of the abdominal wall) than the dorsal soma (i.e. skin, muscle and periosteum of the spine and paraspinal regions). This may offer an advantage to be exploited when applying the conditioning stimuli, i.e. ventral stimulation may have a better effect in modulating visceral sensation and activity. The experimental work of the research group led by professor Akio Sato seems to support this idea (Sato et al., 2002). So for the bladder, often the most convenient and arguably the best approach would be to needle lower rectus abdominis to cover the thoracolumbar segments (T11–L2), and leg points to cover S2 and S3 (S4 is not accessible except in the perineum) – see [Figure 7.2](#). As an alternative, nearly all myotomes can be reached with a dorsal approach, although the convenient muscle of multifidus fades away by about the S3 sacral foramina. The dorsal approach often targets multifidus because the muscle is short and a convenient rule of thumb says that it is innervated at the level of the nearest spinous process. This simplifies choosing the correct level, even though multifidus is a smaller target than the large bulk of erector spinae, which may be innervated up to two segments away from its anatomical level. Each multifidus is actually innervated at the level of its upper vertebral attachment (Bogduk, 1997), and overlaps its neighbours, so at any given level of needling several segments may be stimulated. For example, a needle inserted at the level of the spinous process of L3, one fingerbreadth from the midline, will stimulate the dorsal myotomes of L3, L2 and L1 in that order from superficial to deep if all three fascicles are hit. A more reliable way of hitting the intended segmental level, and indeed safer anatomically in the thoracic spine, is to angle the needle toward the side of the spinous process, where the periosteum is innervated at the level of the nerve of the same designation. For example, the spinous process of L3 is innervated by the medial branch of the dorsal primary ramus of the L3 spinal nerve, which exits the spinal canal through the foramina between the L3 and L4 vertebrae. The muscle that is needed at this site is likely to be multifidus attaching to the caudal surface of the spinous process above i.e. the myotome of L2. When it comes to needling over the sacrum, if the target segment is sacral, then it is wise to place the needles onto the surface of the sacrum itself, as the muscle here is innervated by L3–L5 from lateral to medial (Bogduk, 1997).

## Clinical points

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For conditions in structures innervated by the ventral root of the nerve, treat the ventral parts of the segment; similarly for dorsal root involvement.

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## Small print and fallacies

When discussing treatment of visceral conditions, practitioners often get drawn into the functional distinction between sympathetic and parasympathetic efferent nerves. It should be noted, however, that acupuncture acts through stimulation of afferent nerves and there is no established link between the level of afferent input to the cord and the functional consequence in terms of visceral activity. Acupuncture is likely to modulate activity most effectively at the level of the stimulus, but if there is no abnormal activity at that level then there is unlikely to be any particular consequence. So the best approach is to cover all possible segments involved with the hope of modifying activity where it is abnormal, and without being concerned that anything will happen at other levels. I think it is unhelpful to refer to ‘sympathetic points’ or ‘parasympathetic points’ in this regard.

## Clinical points

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Needling of acupuncture points probably modulates the autonomic nervous system rather than having specific ‘sympathetic’ or ‘parasympathetic’ actions.

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The final small print in this section concerns the sympathetic innervation of the soma. In some chronic pain states sympathetic nervous system activity is implicated as part of the pathophysiology, by either setting up or maintaining the condition. In these cases, practitioners may choose to add to the treatment the segmental levels at which the autonomic fibres exit to innervate the area concerned. These levels can be quite different from the normal somatic segments. In particular it is worth noting that the autonomic innervation of the upper limb is from the segments T2–T9. So in cases of chronic upper limb pain where abnormal autonomic activity is implicated (e.g. chronic regional pain syndrome), as well as using segmental somatic regions (usually in the limb girdle muscles), thoracic paraspinal needling may be added. This is done on a purely theoretical basis.

## The general approach (i.e. non-segmental acupuncture)

### THE IMPORTANCE OF DOSE

The strength of needle stimulation used in acupuncture treatment or dry needling is modified principally according to the immediate response of the patient. The aim is to generate some sensation from needling deep tissues or to obtain an LTR and pain recognition from needling a trigger point, but ideally not to cause unnecessary discomfort. An impression of dose is gained from the great range of immediate responses, and from the range of therapeutic responses, but the nature of any dose–response relationship in acupuncture is not clear (White et al., 2008a). In the laboratory, the dose–response relationship is clearer, and it seems that the stronger the stimulus the greater the effect, at least in terms of pain threshold changes (Huang et al., 2002; Kawakita and Funakoshi, 1982; Pomeranz and Paley, 1979; Romita et al., 1997; Schliessbach et al., 2011; Toda, 2002; Wen et al., 2007; Wu et al., 1974). In clinical studies in humans this relationship is not so clear, and this may be because of relatively large effects in sham acupuncture groups in clinical trials. It is interesting to note that sham acupuncture techniques would generally have no measureable effects in laboratory experiments on stimulation induced analgesia.

## Clinical points

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A dose–response relationship is more in evidence from laboratory studies than clinical trials.

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My impression is that there are different thresholds for effects in different individuals, and some need considerably more stimulation than others. I also have the impression that in peripheral somatic pain complaints, EA appears to have more potent effects as judged by patient preference than manual acupuncture (with minimal needle stimulation).

In an early systematic review of acupuncture in chronic pain, trials using six or more treatments were significantly more likely to be associated with a positive result (Ezzo et al., 2000), though this remains to be tested by direct comparison. Research on *de qi* sensations has failed to yield clear results, perhaps by virtue of the variable nature of this phenomenon and variations in individual perceptions and descriptions. A large individual patient data meta-analysis with meta-regression of acupuncture for pain conditions identified very few characteristics of treatment associated with response (Macpherson et al., 2013), but the number of needles used appeared to be significant when analysing the difference between acupuncture and non acupuncture controls, but not against sham. In a sensitivity analysis, excluding trials that were outliers based on having larger than average effect sizes, the use of EA was associated with the size of effect when acupuncture was compared with sham. Both these factors suggest a dose effect in clinical trials, but the results have to be considered rather speculative at this stage.

## THE ROLE OF BODY REGIONS BEYOND SEGMENTATION

Stimulating different body regions can have different effects, although objective data is limited in this regard. Pleasant sensations derived from stroking hairy skin are processed in different parts of the brain (limbic structures via C tactile afferents) compared with stroking of glabrous skin (somatosensory cortex via A-beta afferents) (McGlone et al., 2012). Stroking of the neck and withers of dairy cows (areas used in social grooming) reduced avoidance and increased approach reactions to humans as compared with the lateral chest or no contact (Schmied et al., 2008).

There is a somatotopic organisation of gentle touch processing (via C tactile afferents) in the posterior insular cortex (Björnsdóttir et al., 2009). Stroke speed also has an influence, with the optimal speed being around  $3 \text{ cm s}^{-1}$  (Morrison et al., 2011), which appears to be more consistent in men. This slow speed of touch may promote a sense of body ownership compared with fast touch (Crucianelli et al., 2013).

Pinching of a rat forepaw or hindpaw and brushing of a hindlimb for 10 min produced significant increases in extracellular acetylcholine release (parietal lobe of cerebral cortex), whereas pinching of the face or back and brushing of the face, forelimb or back produced no significant changes (Kurosawa et al., 1992). Extracellular acetylcholine release appears to correlate with cerebral blood flow (Kurosawa et al., 1989a,b), and can be stimulated by walking (Kurosawa et al., 1993). Baseline levels are highly dependent on cholinesterase activity (Kawashima et al., 1994). These data may be compatible with the idea that increased cerebral blood flow mediated by walking activity may be principally dependant on somatosensory inputs from the hindlimb, and this is one possible mechanistic hypothesis for the observation that regular walking seems to stave off the onset of dementia (Abbott et al., 2004; Vogel et al., 2009; Weuve et al., 2004).

### Clinical points

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It is possible that needling different regions of the body can result in subtly different responses in the CNS.

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These differences raise the possibility that needling different regions of the body may have different effects in a general sense beyond the explanations related to segmental arrange of sensory nerves.

## THE RELEVANCE OF POINTS

So to acupuncture points... At the start of this chapter I referred to MTrPs only being 'points' because they tend to be smaller than the examiner's finger, whereas in reality there appears to be multiple foci of sensory or motor dysfunction in these sites. The practice of acupuncture aims

to achieve a typical perceived sensation (*de qi*) by targeting specific anatomical locations with a filiform needle. The use of the needle both defines the practice and focuses attention on the point of penetration through the skin. So points exist because the needle is used as a tool to apply stimulation, and not the other way around. Points do not exist in the absence of the needle. That is a simple but profound statement, and the failure to appreciate this has led to huge problems in acupuncture research.

### Clinical points

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An 'acupuncture point' does not have any fixed structure but is a useful concept for communication and teaching.

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No universal anatomical substrate has been found at acupuncture points, although numerous theories abound. Nerve bundles, vessels penetrating fascia, motor points, trigger points all seem to be candidates, but no single entity or combination has ever been shown to correlate reliably. A correlation has been identified between meridians in the upper arm and fascial planes ([Langevin and Yandow, 2002](#)), and this idea gains support from the historical records that describe careful palpation of the live body as an important aspect of medical enquiry in ancient China ([Hsu, 2005](#); [Kuriyama, 1999](#); [Lloyd and Sivin, 2002](#)). It seems likely that many, but not all points were found by palpation, and that the reaction of the patient on needling may have been a secondary factor.

While a needle does go through a discrete point, the needle tip may touch a larger area and indeed volume of tissue through movement and altered angulation. Eliciting reactions at trigger points may give the impression that points can be precisely located, since millimetres can make the difference between feeling nothing and eliciting an LTR with pain recognition. However, clinical research in chronic pain conditions suggests that precision of needle location is mostly unimportant in eliciting effects ([Haake et al., 2007](#); [Linde et al., 2009](#); [Vickers et al., 2012](#)).

So if points do not exist in the absence of the needle, why do we continue to teach them? Well some teachers do not ([Campbell, 1998](#); [Mann, 2000](#)), but in my experience, the majority of health professionals learning acupuncture in short postgraduate courses benefit from learning a limited number of the commonly used locations for needling as classical points when they start using the technique. The nomenclature of points makes them easier to note than the anatomical target, e.g. ST36 versus around the middle of tibialis anterior. If you limit your practice to a number of defined areas initially, this reduces the amount of somatic anatomy you need to revise or learn. Finally, for some patients the context of acupuncture treatment can be strongly associated with the use of certain points, and the context of care can have powerful effects to either enhance or negate the specific physiological effects of treatment ([Benedetti et al., 1999](#); [Bingel et al., 2011](#)).

## Contextual factors

### WHAT IS MEANT BY 'CONTEXT EFFECTS'

Context effects can be defined as the effects of a therapy that are derived from all aspects of the environment, the patient's background and their interaction with a therapist, apart from what is regarded as the specific effects of an intervention. The demarcation is less clear in physical medicine than it is in drug treatment. In terms of acupuncture, the physiological effects of the needle (in any somatic tissue irrespective of points used) can be considered to be specific effects, and other aspects of care can be considered contextual. Of course acupuncture treatment may include stretching exercises, lifestyle and ergonomic advice, and cognitive interventions, and these may be considered specific to the treatment approach. Contextual effects relate to general aspects of care that are present and unrelated to the specific intervention, though may vary with different interactions and circumstances. Changes over time may be unrelated to the therapy or the context

**BOX 7.2 ■ Context effects**

- Environment
  - Physical environment
  - Time
- Practitioner
  - Physical appearance
  - Verbal communication
    - Practitioner expectation
    - Cognitive reassurance
  - Non-verbal communication
    - Facial expression
    - Posture
    - Demeanour
    - Touch
  - Empathy
  - Compassion
  - Therapeutic alliance
- Patient
  - Conscious
    - Expectation
    - Cognitive changes (either directed by the practitioner or undirected)
    - Attention to sensory discrimination aspects of therapy
  - Unconscious
    - Conditioning
  - Summative aspects
  - Relaxation versus anxiety

*This list is intended as a guide to the different aspects of context, and there are clearly overlaps and interactions that cannot be easily represented in this simple format.*

of care, hence the importance of untreated control groups in clinical trials. The natural history of the condition may influence changes over time.

Context effects can be divided (for the sake of making a simplified list) into those related to the environment, those related to the practitioner and those related to the patient (Box 7.2).

## ENVIRONMENT

### Physical environment

The physical environment of the healthcare setting appears to affect the wellbeing of patients, with sunlight, windows, odour and seating arrangements generally producing positive effects in trials (Dijkstra et al., 2006). Music has also been associated with generally positive effects, although the data are not fully consistent (Biley, 2000).

### Time (and how it is used)

Perceived length of consultation, rather than actual length, has been associated with increased satisfaction in general practice (Cape, 2002; Lussier and Richard, 2007). Small changes in consultation time do not seem to correlate with useful healthcare outcomes (Wilson and Childs, 2006), and patients' perception of the availability of time may be more important than the actual length of consultation in some settings (Pollock and Grime, 2002). There may also be an advantage to allowing unrestricted initial spontaneous talking time (Langewitz et al., 2002).

Acupuncture consultations tend to be longer than general practice consultations, and tend to be less pressured in terms of achieving consultation-related outcomes, so this alone may promote positive affect, relaxation and anxiety relief.

## PRACTITIONER

### Physical appearance

The majority of the research in this area seems to focus around doctors and white coats. In general the formal medical attire is associated with increased patient confidence (Gherardi et al., 2009; Gooden et al., 2001; Rehman et al., 2005), and may promote improved practitioner–patient interactions (Chung et al., 2012). This effect seems to be apparent in both Eastern and Western countries (Landry et al., 2013; Sotgiu et al., 2012; Yamada et al., 2010), but has not been demonstrated in all settings (Fischer et al., 2007). It also seems to be independent of the style of medicine practised (Chang et al., 2011). Attire is just one aspect of physical appearance, and it is likely that other aspects such as gender differences and age differences between practitioners and patients affect attitudes and interactions that contribute to the context of care.

### Verbal communication

Practitioner (communication of) expectation was associated with outcomes in an acupuncture trial of osteoarthritis (Suarez-Almazor et al., 2010), although this was on the background of rather a small change from baseline in the acupuncture groups. Rather more data comes from an analysis of pragmatic RCTs (Acupuncture in Routine Care – ARC studies) that were part of the Modellvorhaben Akupunktur (Cummings, 2009). Data from four of the ARC studies (Jena et al., 2008; Witt et al., 2006a–c), relating to 9900 patients treated by 2781 physicians, was reanalysed to investigate the effect of physicians' expectations on treatment outcome in acupuncture and usual care (Witt et al., 2012). High expectations of physicians correlated with a better treatment outcome after adjusting for a multitude of patient characteristics, although the effect was small.

Cognitive reassurance (providing explanations and education), as opposed to affective reassurance, in primary care consultations seems to be associated with higher patient satisfaction and enablement and improvement of symptoms (Pincus et al., 2013). This is veering to some degree from the context of care to a specific cognitive intervention, however, this is likely to be judged from the reference point of the assessed intervention.

### Non-verbal communication

Acupuncture studies have revealed a prominent practitioner effect, and this effect cannot be explained entirely by verbal communication. Indeed the practitioner effect in one study appeared to be twice as big as that attributed to the consultation style (Kelley et al., 2009). It seems likely that this effect relates in some way to non-verbal (animal, limbic) communication (see discussion in the succeeding text).

Therapeutic touch has shown moderate effects, and reviews mostly consider effects on pain (Monroe, 2009; Peters, 1999; Winstead-Fry and Kijek, 1999). Presumably part of the mechanism for an effect on pain is through target-directed expectation (Benedetti et al., 1999), which is discussed further in the succeeding text.

### Empathy, compassion and therapeutic alliance

Empathy is the capacity to feel the emotions that are being experienced by another, whereas compassion refers to the awareness of suffering of another, and tends to generate active support. The therapeutic alliance refers to the relationship between a healthcare professional and a patient,

which aims to bring about a positive change in the state of the patient. They are interrelated aspects of effective patient-centred care, and there is evidence for a moderate effect on healthcare outcomes (Elliott et al., 2011; Lelorain et al., 2012; Martin et al., 2000).

In acupuncture trials of climacteric symptoms (unpublished work from Borud et al., 2009a,b), irritable bowel syndrome (using only a non-penetrating sham (Kaptchuk et al., 2006; Kelley et al., 2009)) and osteoarthritis (White et al., 2012), large practitioner differences in outcomes have been recorded (up to a threefold difference). These differences are apparent even when controlling the verbal interaction (augmented vs. limited consultations (Kelley et al., 2009; White et al., 2012)). Differences in consultation style did have significant effects (Kaptchuk et al., 2008), but the practitioner effect (independent of style) was twice as big (Kelley et al., 2009). This suggests that non-verbal aspects of the interaction may have been more important than verbal ones in this setting and for the outcomes measured, and it is intriguing to consider whether the difference relates to involvement of neocortex (language and analysis) rather than paleocortex (limbic, non-verbal, animal).

## PATIENT

### Expectation

Positive expectation of the efficacy of an intervention is thought to be a key component of the placebo effects (Colloca and Miller, 2011). Similarly, negative expectations can generate nocebo effects (Colloca et al., 2008). Nocebo effects may be more powerful in general, and in one notable experimental trial the effect of an intravenous opiate infusion (in terms of both pharmacological and positive expectation of analgesia or placebo) was almost entirely reversed (subjective assessment and fMRI changes) by the negative expectation of being told the infusion had been stopped (Bingel et al., 2011).

In clinical studies of acupuncture, patient expectation of outcome has been associated with better outcomes, but not in all circumstances. Data from the four acupuncture randomised trials of the Modellvorhaben Akupunktur (Cummings, 2009), which included 864 patients with migraine, tension-type headache, chronic low back pain or osteoarthritis of the knee, were analysed for an association between patient expectation (assessed after three acupuncture treatments) and outcome (Linde et al., 2007). The results showed that patients with positive expectations were twice as likely to respond to treatment. One limitation is that good responders to acupuncture would already have an idea after three sessions that there was a benefit. In a study of acupuncture and massage in low back pain, higher expectations correlated with better functional outcomes, and patients who expected greater benefit from massage than from acupuncture were more likely to experience better outcomes with massage than with acupuncture, and vice versa (Kalauekalani et al., 2001). Interestingly, a subsequent trial from the same group on acupuncture for back pain did not find any effect of expectation or preferences on outcome (Sherman et al., 2010), although another group in the United States did find an effect of expectation on functional outcomes in acute back pain (Myers et al., 2008).

Outside the realm of acupuncture research, no effect of patient expectation was found in total knee and hip arthroplasty (Haanstra et al., 2012).

*Target-directed expectation* was described within experimental research on placebo mechanisms (Benedetti et al., 1999). The pain induced by capsaicin injections in all four limbs was abolished in one limb when placebo anaesthetic cream was applied; this effect was completely reversed by prior naloxone injection. Opioid mechanisms appear to be involved in this targeted placebo effect. While a placebo cream was used in this study, a similar mechanism of somatotopic activation of opioid systems may be generated by local application of acupuncture or sham acupuncture in an area of pain.

## Cognitive aspects

Of course, cognitive analysis of the setting and circumstances is likely to be an important factor in the development of expectations related to an episode of care. But there may be other cognitive processes that contribute to satisfaction and enablement (Pincus et al., 2013).

## Sensory discrimination

Another aspect of the experience of having needles inserted into an area of pain is the spatial location of the needle sensation and discrimination between different needle sensations. The practitioner who enquires about needle sensation as different needles are stimulated may unconsciously drive this aspect of treatment. Sensory discrimination training during an acupuncture intervention has been studied in back pain, and an augmented form of training during needling proved to have a significant influence on motion-related pain immediately after the intervention (Wand et al., 2013).

## Conditioning

Conditioning procedures are often used in placebo studies of acute pain to produce more robust effects (Colloca et al., 2010), but it is likely that conditioning also plays a part in the treatment effect that occurs in normal clinical practice. Both small specific effects of needling and various context effects may contribute to responses that are conditioned to the unique environment of the acupuncture treatment experience, thus reinforcing the effect over repeated treatments. This may be part of the reason that sham acupuncture procedures appear so much more effective than placebo pills (Kaptchuk et al., 2006; Linde et al., 2010; Lundeberg et al., 2007).

## Relaxation versus anxiety

Most (but not all) of the aspects of context discussed earlier relate to or are mediated by some form of cognitive appraisal of self in relation to the environment. That appraisal can result in the individual having either a heightened or lowered level of anxiety. Anxiety (e.g. generated through negative expectation) has been shown to antagonise opiate mediated analgesia (Bingel et al., 2011), and this seems to be mediated through activation of CNS cholecystokinin (Benedetti, 2008; Colloca and Benedetti, 2007). Responsiveness to acupuncture analgesia appears to be influenced by cholecystokinin levels in the CNS, as does placebo analgesia (Zhao, 2008), so it seems likely that they share a common mechanism.

## Concluding comments

This chapter describes a variety of acupuncture needling approaches guided by mechanisms, which are the basis of Western medical acupuncture. Much of the information and advice is based on interpretations from basic science and experimental research. Local approaches, segmental relations and the general aspects of needling are included. The final discussion on context effects attempts to dismantle the architecture of the clinical interaction in acupuncture treatments, and underlines the enormous complexity of different interacting and overlapping effects that create the challenge for clinical research into the efficacy of acupuncture. From the pragmatic perspective, clinicians' wielding of fine needles appears to be a powerful therapy, and this chapter tries to offer both guidance and perspective.

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# Acupuncture without points

A. Campbell

## CHAPTER OUTLINE

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## Introduction

Probably the commonest question that acupuncturists receive from both beginners and more advanced practitioners is ‘Which points do you use?’ The implication is that needle location is what matters most. And there is a natural transition from this to the idea of ‘advanced acupuncture’, which presumably would depend on the use of unusual points or complicated combinations of points. Becoming an acupuncture expert, on this view, is largely a matter of learning more and more points, but that begs a number of questions.

The point concept is based on Chinese traditional ideas and postulates the existence of specific sites at which needles should be inserted to produce various therapeutic effects. There have been numerous attempts to investigate points scientifically. These have included histological studies, but probably the commonest approach has been to measure the electrical conductivity of the skin over the points. Few convincing results have been obtained in these ways, and looking for changes in skin conductivity can be criticised on the grounds that the classic points are supposed to lie at some depth within the tissues; it is not obvious why there should be skin changes overlying them.

## Do acupuncture points exist?

There are good reasons for doubting the existence of points as traditionally described. The fact that needling a given site relieves particular symptoms or produces other physiological effects does not prove that the point in question really exists and has specific therapeutic properties not shared by other sites. That would require demonstration that the same effects are not also produced by needles inserted elsewhere. In practice, this is difficult to do. How far away should the ‘incorrect’ insertion be? How deep? Are the needles to be stimulated in any way, and, if so, how can this be done equally at the two sites? And how can the practitioner, who presumably knows the ‘correct’ site, avoid unconscious bias in performing the treatments?

In spite of such difficulties, belief in the existence of points has prompted numerous clinical trials to compare the effects of acupuncture at classic sites (true acupuncture) with acupuncture

done at other sites some distance away from the ‘correct’ sites (the so-called sham acupuncture) (Witt et al., 2000; Linde et al., 2006; Scharf et al., 2006; Kim et al., 2011). With a few exceptions, studies of this kind have found little evidence for a significant difference between real and sham treatments. This presumably means either that most acupuncture responses are due to nonspecific causes, including the placebo effect, or else that needle insertion does have a therapeutic value but it often makes relatively little difference exactly where the needles are inserted.

A number of practitioners have become convinced by their clinical experience that the traditional view of points is not valid. The first to publish his conclusions on this was Felix Mann. He began his acupuncture career as a traditionalist but later changed his view (Mann, 2000). He came to disbelieve in the existence of points, having found that for many patients the exact location of needles was unimportant and it was better to think in terms of areas rather than points. In an attempt to escape from the traditional terminology he went so far as to develop his own nomenclature to describe needling sites, so that, for example, he renamed LR3 ‘dorsalis pedis/dorsal interosseus area’ (abbreviated to DPDI). But this rather cumbersome terminology does not seem to have been widely adopted by others.

Given that there is considerable doubt about the existence of points as traditionally conceived, are there any reasons to ask newcomers to acupuncture to learn their locations? Some practitioners who fully adhere to neurophysiological explanations for acupuncture believe that there are (White et al., 2008). It is said that *de qi* is usually easy to elicit at acupuncture points and that certain points appear repeatedly in traditional ‘prescriptions’ for treating various symptoms, which suggests that they may have widespread effects.

Cheng has shed light on the traditional idea of points in a recent study (Cheng, 2011). Rather than concentrating on individual points and their alleged effects, he looked at the distribution of groups of points in the traditional Chinese literature to see how they relate to the areas of the body they are used to treat. He found evidence for three kinds of clustering. First, internal organs tended to be related in a segmental manner to points on the trunk. Second, musculoskeletal effects were attributed to local or regional points but not to distal ones. Third, points on the head and neck were used to treat the nearest organ. These findings seem to indicate that choice of where to needle is based on local, regional or segmental considerations rather than on the precise location of individual points.

Probably the strongest argument in favour of retaining the points is their possible usefulness for recording the treatment. They do offer shorthand descriptions of where the needles have been inserted – provided, of course, that this was done at a named site. In practice, I think it is worth retaining a very small number of names for frequently used sites, though probably not more than half a dozen out of the 360 or so that are commonly listed. But teaching large numbers of points to students is both unnecessary and undesirable. The more points students are confronted with, the more complicated acupuncture appears and the greater the temptation to believe that becoming skilled in acupuncture requires the learning of numerous points and their supposed effects.

Indeed, the term ‘point’ is itself misleading and probably better avoided. It conveys the impression that needling has to be done very precisely, which is seldom the case. To counteract this I prefer to speak of ‘acupuncture treatment areas’. This terminology is intended to encourage a more relaxed attitude to the localisation of needling sites.

## Doing without points

Anyone who is used to the points idea will probably feel somewhat insecure when contemplating its abandonment. How are we to decide where to place the needles if we do not use points? I suggest that the choices can be summarised in four guiding principles – four main methods of deciding where to place the needles. The possibilities are as follows:

Method 1. Needle the affected area (site of pain) itself. Method 2. Needle the periosteum (mainly though not exclusively for joint pain). Method 3. Needle a remote site that may influence the affected area. Method 4. Needle to produce centrally mediated effects.

I shall now expand this summary to explain how the scheme works in practice. Note that although it is convenient to describe the possibilities under these four headings, there is some overlapping among them, and there is no reason why the different approaches should not be combined; in fact, they often are.

## METHOD 1: NEEDLE THE AFFECTED AREA ITSELF

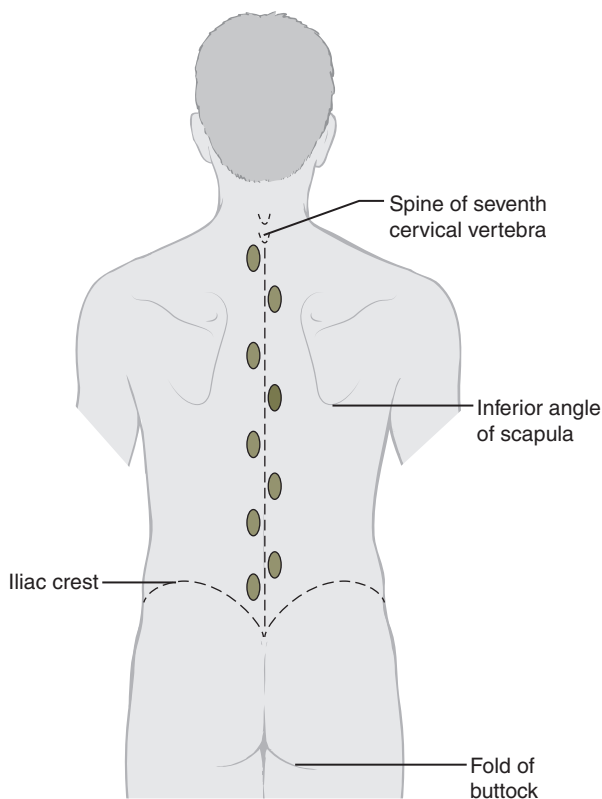
This is the simplest form of acupuncture and is often all that is needed. Inserting needles into the tissues causes the release of various neuropeptides, notably calcitonin gene-related peptide, which is a potent vasodilator and is involved in the transmission of pain (White et al., 2008). Recently, adenosine has been added to the list: this is a neuromodulator with antinociceptive properties that has been shown to be released during acupuncture in an experimental pain model in mice. Direct injection of an adenosine A1 agonist replicates the analgesic effect of acupuncture in this model, and inhibiting the action of enzymes that degrade adenosine potentiates the acupuncture response (Goldman et al., 2010).

However, although these local effects occur and are important, that does not necessarily mean that the whole effect is produced locally. For example, scar pain can usually be cured by direct needling into the scar at sites of tenderness. While local effects may be relevant here, a more complete explanation will probably include the phenomenon of *pain memory*. This implies that the persistent pain in these cases, and in other types of chronic pain, is due to long-term changes in the spinal cord and brain centres. These could include reverberating neuronal circuits, the formation of new interneuronal connections, or sprouting of new nerve fibres. Alterations in the balance between long-term potentiation and long-term depression may also be important (Sandkühler, 2000; Ru-Rong et al., 2003; Sufka, 2000; Malcangio and Lessmann, 2002). Probably an important way in which acupuncture works in chronic pain is by modifying pain memory. Thus local treatment, although seemingly simple, may actually have complex far-reaching effects.

Classical acupuncture points have little relevance to this kind of treatment. Even when an area to be treated contains classical points there is no particular advantage in needling them selectively. For example, in the treatment of widespread spinal pain, due perhaps to ankylosing spondylitis or osteoporosis, it is unnecessary to select traditional Bladder points (or trigger points (TrPs), for that matter). Doing so will work, but the results appear to be equally good if the needles are simply inserted in the paraspinal muscles at roughly 2-cm intervals, with no further attempt at precise localisation. For convenience a zigzag pattern may be used (Fig. 8.1).

## METHOD 2: NEEDLE THE PERIOSTEUM

This technique does not seem to be practised to any extent in the traditional system and is unrelated to classical points. It was introduced by Mann (Mann, 2000) and is a good resource for treating intrinsic joint pain such as that due to osteoarthritis or inflammatory or reactive arthritis (provided it is not too acute). As the name implies, it consists in quick (2–5 s) ‘pecking’ of the periosteum in the region of the joint. (Joints should not be needled intra-articularly for fear of causing a septic arthritis.) There is no need to look for specifically tender areas. It is not clear how far from the joint the needle can be placed without losing effect but certainly it does not have to be directly adjacent. Periosteal needling typically produces a deep, rather unpleasant, ache, although some patients do not feel it at all. How it works is unclear but it probably depends on central effects in the spinal cord.



**Figure 8.1** Treatment areas in the paraspinal region.

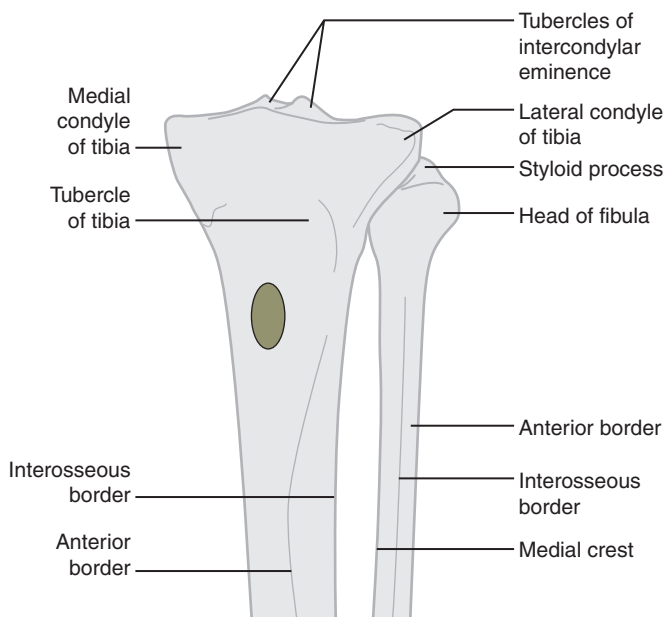
The effectiveness of brief stimulation of this kind may be surprising but it is supported by clinical experience and, to a limited extent, by experimentation (Marcus, 1994), though this study was on soft tissue, not periosteal, needling.

Any joint can be treated in this way, the only criterion being safety; no important structures should be penetrated on the way in to the periosteum. A good example is treating the knee by needling the flat area on the tibia below the medial condyle. Another site that is frequently used for arthritis of the hallux is the first metatarsal; this can be needled using an area between the tendon expansion dorsally and the vessels and nerve laterally and medially (Fig. 8.2).

Although periosteal needling is mainly used for joint pain the same technique can be applied for other purposes, such as treatment of an enthesopathy. For example, in most patients plantar fasciitis responds well to needling the attachment of the plantar fascia to the medial calcaneal tubercle. Ankle sprains can be treated similarly: the needle is applied to the attachment of the anterior talofibular ligament.

Certain periosteal sites can influence a wide area of the body. Examples are the articular pillar in the neck, which can influence pretty well anything in the upper half of the body, and the region of the sacroiliac joint, which can be used to treat referred pain in the lower limb (Mann, 2000). Incidentally, needling the sacroiliac region can alleviate scrotal pain and pain in the lower abdominal quadrant, although it is obviously essential to eliminate serious organic disease in such cases. Acupuncture is a symptomatic treatment and the fact that it relieves symptoms is not evidence that no serious pathology is present.

Periosteal needling is a nontraditional treatment and has nothing to do with classical points.



**Figure 8.2** Area for periosteal needling for knee pain.

### METHOD 3: NEEDLE A REMOTE SITE THAT MAY INFLUENCE THE SITE OF PAIN

This method may appear to have more similarity to the traditional approach but I think this is true only to a very limited extent. The use of remote sites to treat painful areas depends on the referred pain phenomenon. (In some cases, symptoms other than pain, such as altered sensation, are what need treatment, but the same principles apply.) The commonest cause of referred pain is TrPs (including myofascial trigger points, MTrPs). In some cases classic acupuncture points correspond to known TrPs, and possibly this is how some classic points were discovered originally (Baldry, 1998), but that does not mean that the use of traditional terminology in such cases is desirable. It is more informative, and usually more accurate, to use conventional anatomical descriptions of where the needle is inserted. It is also possible to mark the site that has been needled on a printed body outline chart, but this is seldom accurate enough and the muscles are not usually depicted.

A good example of the unsatisfactoriness of traditional terminology is GB30, traditionally used to treat referred pain in the lower limb (sciatica). But this is a surface marking, and what we are really interested in is MTrPs situated in the deep gluteal muscles, such as piriformis, gluteus medius or gluteus minimus. Tenderness in these muscles is elicited by palpation and the surface marking of GB30 adds nothing useful.

The case for GB21 as a named point may be a little stronger. It is situated over the midpoint of the trapezius, and is at least a latent MTrP in almost everyone; it frequently becomes activated and gives rise to neck or arm pain. It is therefore not unreasonable to use GB21 as a shorthand description of where the needle has been inserted, and failure to do so may confuse some readers since it is such a well-known classic point. But there is a risk that this will focus the mind too precisely on a particular location, whereas what is really important is the identification of MTrPs, of which there may be more than one in the region. There is often a MTrP at the junction between the neck and shoulder in levator scapulae, which is reached through the fibres of trapezius. This is not a classic point but is nevertheless worth knowing about and treating if necessary. If GB21 is used as a shorthand term, therefore, the fact that it is just a rough guide to where to needle rather

than a rigid prescription needs to be understood. MTrPs are commonly found in the neck muscles of the posterior triangle (splenius capitis and splenius cervicis) but these do not correspond to classic points.

Not all forms of remote needling depend on TrPs. Segmental acupuncture, in which needles are inserted in relevant dermatomes, myotomes or sclerotomes, also constitutes remote needling and sometimes it may be convenient to use traditional terminology in such cases. For example, SI3 is recommended for upper thoracic pain and does appear to work for this. Probably it does so because it is in the C8 dermatome and the C8/T1 myotomes.

Although much remote needling can be explained in terms of TrPs or spinal segments, that is not always true, and in such cases there are presumably other central pathways that are as yet unknown.

## METHOD 4: NEEDLE TO PRODUCE CENTRALLY MEDIATED EFFECTS

In some patients, acupuncture can produce widespread therapeutic responses that appear to be centrally mediated. Although almost any site may have such effects, particularly in those people who respond strongly to acupuncture, certain areas seem to be particularly effective in this respect. These are mainly in the hands and feet. LI4 is widely used in this way but it is usually painful and on occasion has adverse effects, including thrombosis of the radial artery. I have seen a case of pain in the thumb lasting for 6 months after this site was used. LR3, in contrast, is safer and less painful than LI4 and is probably more effective.

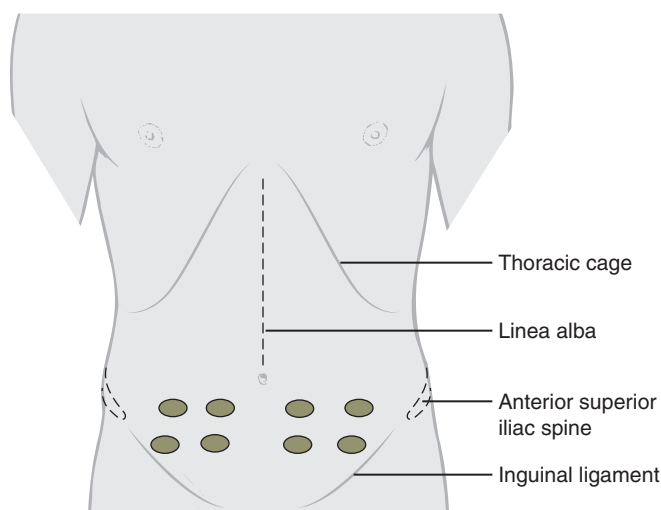
LR3 is described as situated on the dorsum of the foot in the first interspace, but how critical is this location? Would a different interspace work equally well? Anywhere on the foot? Anywhere below the knee? There are probably some patients in whom any of these sites would have an equivalent effect, which may explain why some practitioners report widespread effects from using other leg sites, such as ST36. Still, the name LR3 provides a useful shorthand description and is preferable to neologisms such as DPDI. The treatment can be performed bilaterally but there often appears to be a difference in effectiveness between the two sides, with more patients responding more strongly on the left. (This has nothing to do with the degree of left or right dominance.) It is, therefore, best to begin with the right side in case the patient turns out to be an exceptionally strong reactor.

There may be unusual effects in some people. A degree of relaxation is quite common, and this can go on to become frank euphoria. Some patients remark that everything seems brighter. Laughter or tears may ensue. Occasionally patients appear to have difficulty in speaking while being needled and other strange mental states occur from time to time. At least some of these are probably limbic system effects (Campbell, 1999).

This method can be used in a wide range of disorders, especially in strong reactors. Among conditions that may respond are migraine (especially if preceded by an aura), chronic urticaria, polymorphic light eruption, menopausal hot flushes, and, occasionally, bronchial asthma (although acupuncture is generally unsuccessful in asthma, there are a few patients who do outstandingly well, with large sustained increases in peak flow - personal observation). The treatment may be used on its own or to reinforce the effect of needling other sites.

## Qualifications

The classification of treatments advocated here seems to be useful for clinical purposes as a descriptive scheme but it should not be interpreted too rigidly. Difficulties in classification arise in relation to the treatment of internal organs. For example, subcutaneous needling over the lower abdomen can be effective for abdominal pain and other symptoms, including those due to



**Figure 8.3** Treatment areas used for abdominal problems.

inflammatory bowel disease, especially ulcerative colitis. This could be thought of as local treatment, since the needles are inserted in the affected area. But it could also be classed as segmental, since the spinal nerves have branches both to the abdominal muscles and the internal organs (Carlsson, 2002). A third possibility is centrally mediated neurohumoral effects. Hence this treatment could be regarded as using Method 1 or Method 3, and in either case Method 4 might also be involved (Fig. 8.3).

How to choose which method or methods to use in different cases is outside the scope of this discussion, but the decision will turn on consideration of the nature of the underlying problem. For example, pain in a joint may be due to intrinsic disease such as arthritis, but it may also be referred from elsewhere. In the first case Method 2 (periosteal needling) would probably be indicated, while in the second Method 3 would be appropriate and would probably require the identification of MTrPs.

## Concluding comments

Acupuncture has had a long history in the West since its first description by a Dutch physician, Wilhelm ten Rhijne, at the end of the seventeenth century. It began to be used by European physicians and surgeons at the beginning of the nineteenth century, but this was with little reference to Chinese ideas. For the most part the needles were simply inserted at the site of pain (Method 1). Many doctors used acupuncture at this time and it might have continued to be an accepted form of therapy into modern times, but this did not happen. The reason was a change in outlook which occurred in the first half of the twentieth century, largely owing to a Frenchman, George Soulié de Morant (1878–1955). He went to China in 1901 to work in a bank and acquired a deep interest in Chinese medicine, especially acupuncture. On his return to France he practised the treatment and advocated it enthusiastically. He translated some texts and taught acupuncture to both doctors and people without a conventional medical training. As a result of his work acupuncture in the West became much more traditional, with an emphasis on the points as well as on other traditional concepts including *qi*.

The view of acupuncture put forward by Soulié de Morant did much to shape how many Westerners came to understand acupuncture. It certainly made acupuncture appear esoteric and

unscientific to most health professionals in the West in modern times. As a result it was largely ignored in mainstream medicine until fairly recently, but that is now changing. Acupuncture today is increasingly being seen as a treatment worthy of research and incorporation into clinical practice. We now have an abundance of clinical experience to support its use as a therapeutic modality and there is an increasing quantity of research evidence to show how it works. What we do not have is much evidence for point specificity. The question therefore arises: is it time to abandon the points terminology, as Mann did in the 1970s?

Doing so has a number of advantages. For newcomers it simplifies the learning of acupuncture without oversimplifying it. In fact, it probably makes them think more deeply about what they are doing, because it eliminates the temptation to rely on prescriptions or 'acupuncture cookbooks'. Instead of believing that there must exist some obscure selection of points to treat difficult problems, they have to think in terms of pathology and neurophysiology, and this may suggest new methods of using the needles, as it did in Mann's case when it prompted him to introduce periosteal needling.

Abandoning the arcane points terminology seems to be the logical next step in the modernisation of acupuncture. This will hasten its progress from complementary to mainstream treatment, and will avoid the need for confusing terms such as dry needling that seem to have been introduced to differentiate traditional and nontraditional types of needle treatment. All therapeutic interventions that involve the insertion of solid needles may be referred to as acupuncture. Clinicians and researchers can then make progress without being handicapped by concepts that have their roots in a different way of thinking.

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# Superficial acupuncture

A. Macdonald

## CHAPTER OUTLINE

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## Introduction

Need needling always be deep? The answer lies in location. If only the tip of a needle is inserted into skin without rotation or further manipulation at a location far away from a tender region, little if any hypoalgesia tends to occur – so much so, this is sometimes employed as a ‘sham’ in the control arm of a trial, where the intervention requires each needle to be inserted a centimetre or more in the usual Chinese manner into deep tissues to excite neural elements (Dong et al., 1993) lying not only in the skin but also in a sizeable volume of deep tissues wrapped around it in the shape of a ‘whorl’ (Langevin et al., 2001). Here the practitioner not only rotates the shaft of the needle this way and that but moves it up and down to produce *de qi*, a term describing one or more of the following rather unusual sensations reported by the patient that are considered to be a vital part of a successful acupuncture treatment: ‘aching’, ‘soreness’, ‘pressure’, ‘fullness’, ‘heaviness’, ‘numbness’, ‘tingling’, ‘warmth’, ‘coolness’ and ‘dull or sharp’ pain (Hui et al., 2010).

However, in the mid-1970s, the author made an unexpected observation. If the skin overlying an abnormally tender region associated with a musculoskeletal condition is needled to a depth of no more than 4 mm without rotation or further manipulation, once the needle is removed a few minutes later – a highly localised reduction in tenderness to palpation may be found in tissues lying immediately below the needle site, even though this procedure fails to elicit *de qi* sensations.

To discover the location where this phenomenon may take place, palpation is required to reveal the surface markings of an abnormally tender region. The importance of such a search was underlined in China by the inestimable doctor, Sun Szu-Mo (AD 581–673), ‘*Needle wherever there is tenderness*’. Tender regions, whether in the vicinity of acupuncture points or not, were accorded the title ‘*Ab shih hsüeh*’ or ‘*Ab Shi*’ – this is where the patient cries out, ‘Oh yes’, in order to warn the doctor not to press any harder (Lu and Needham, 1980). Indeed as Kellgren (1938) described, when a tender region is palpated with increasing pressure, ‘*There is a steep rise in pain ... which causes the patient to wince and cry out*’.

To find such a tender region is not always easy, particularly as tenderness is so subjective. Nevertheless, the practitioner may discover the location of a tender region by exerting a downward pressure of approximately  $1.5 \text{ kg cm}^{-2}$  (Dung, 1984; Macdonald, 1980; Travell, 1976).

Most doctors are taught to exert such a downward force via a stationary examining digit. The recommendation here is to continue supplying the downward force while at the same time adding a shear force to elicit a response from sensitised deep tissues. This is achieved by moving the examining digit sideways over the skin until the boundary of the tender region is reached (Macdonald, 2011).

The thumb is removed as soon as the patient declares the forces employed are becoming painful. An important detail is to trim one's finger nails otherwise the patients will report pain as soon as they are scratched. By sliding the examining finger or thumb sideways from various directions one may determine the extent of the surface markings of the whole region that the patient declares is tender.

Abnormally tender regions often appear in what may seem to be rather paradoxical locations. They are often found in the opposite compartment to that which we were taught to consider as being the most likely. When abduction is painful, tenderness is usually found in adductor regions. In a similar manner, if flexion is painful, tenderness will be found in the extensor compartment.

An explanation is that this is the region where the sensitised deep fascia is stretched by a painful movement. In addition to this, when muscle volume increases during an isometric contraction associated with a forced resisted manoeuvre, its deep fascia is stretched and this tends to elicit pain (Macdonald, 1980).

The author has observed two effects that occur usually within 5 min of inserting a needle superficially into skin overlying an abnormally tender region: these are vasodilatation (see Fig. 34.1) and a marked reduction in tenderness in the deep fascia when the same region is palpated again.

Both of these phenomena tend to be localised to tissues whose surface markings occupy a small oval region extending around the needle itself, a region whose longest axis may only be 1 or 2 cm in length. However many abnormally tender regions in severely affected patients are much more extensive than this. Their surface markings occupy  $50 \text{ cm}^2$  or more. As the effects of one needle inserted superficially usually produces its effects in so small a region, when a large tender region has been found, several needles need to be inserted to produce a continuity of effect over the whole. Each needle is inserted in such a way that it is separated from the next by  $\sim 2 \text{ cm}$ . This forms a pattern of superficial needles covering the whole tender region.

Tenderness may also be found by palpation in a ligamentous region. Here superficial needling also tends to produce localised hypoalgesia when applied to skin overlying it. This is particularly useful in treating tender interspinous ligaments of the spine or where joint penetration should be avoided and one wishes to reduce tenderness in for example a collateral ligament of the knee.

Although tenderness to palpation is markedly reduced within 5 min or so, frequently there is a delay of several hours before the patient (if a responder) notices the benefit. No one knows why this delay should occur. After this, in those who respond, the first treatment produces considerable relief for an average of 12 h. Subsequent treatments produce a progressive duration of relief: for example, the second produces some 24 h or so, while the third 2 or 3 days' relief, etc. To obtain a 60% or more continuous relief for several months, six or seven treatments are usually required. When there is such a long interval between each treatment and the treatment itself is so brief and minimal, why the duration of benefit accumulates in this way is not known. However, if after the third treatment relief has not yet appeared or only lasts but a few hours on each occasion, this does not promise lasting benefit and the course of treatments should be stopped.

During a treatment, the time to remove a needle is the moment when vasodilatation associated with its insertion becomes quite florid in appearance (see Fig. 34.1); this usually occurs within 5 min. Each patient is unique and changes may develop more rapidly or gradually than this. Some patients only require needles to be inserted for a very brief period of time, perhaps a minute or

less. The warning is, if needles have been left in for too long for a particular patient on any occasion, then a worsening of the condition can commence within 48 h after treatment and last for 2 or 3 days. If such a response occurs, then the needles are left in for a shorter period of time on the next occasion. The patient is told about this possibility and taught to pinch the region if worsening occurs.

If the practitioner is able to treat the patient during this episode, inserting one needle superficially into the centre of the exquisitely tender region is enough to produce a very marked reduction in tenderness within a few minutes. Why this should be so is yet another mystery. In order to avoid making the condition very much worse, the treatments should not be performed within 2 days of each other unless one can treat the patient as soon as a worsening of the condition appears. Therefore treatments are usually provided at weekly or, as Felix Mann was the first to suggest, at fortnightly intervals.

One can see the superficial approach presents various disadvantages as compared with the deep.

Additional time is required to find abnormally tender regions, particularly as these are often to be found in unexpected sites that the patient is not aware of until palpation is performed particularly when placed some distance away from the region of referred pain.

More needles are usually required when practising superficial as compared with deep acupuncture. Depending on the size of the tender regions, sometimes 20 superficial needle insertions are made.

Another disadvantage is that needles so superficially inserted tend to fall out altogether and may have to be retrieved from clothing or the floor. Therefore a very careful count of all needles is required.

Superficial acupuncture, however, does present certain advantages over deep acupuncture. It removes the risk of needles being inserted deeply and causing trauma to viscera, joints, major blood vessels and nerve trunks, causing rare but serious events reported by [Peuker and Grönemeyer \(2001\)](#), [Zhang et al. \(2010a\)](#) and [Chou et al. \(2011\)](#). While treating tender regions in the neck or the thorax, for example, this concern about penetrating vessels and other important deeply lying structures is markedly reduced.

Also, as the Japanese found during their development of superficial acupuncture in the seventeenth century, it reduces distress in patients who are anxious about manipulation of deeply inserted needles. The time taken to identify the size and location of all the tender regions is often appreciated by the patient who may declare this is the first time any practitioner has taken such trouble. If on re-palpation immediately after stimulation tenderness is markedly reduced, this gives the practitioner the comfort that something has been achieved even though the patient may not become aware of a benefit for several hours.

## Depth of superficially inserted needles

Whatever its depth, one can determine the needle tip has been inserted superficially and has not reached deep tissues such as fascia investing muscle, when contraction or relaxation of the underlying muscle fails to alter the angle of the needle. In contrast, deep needling almost always invades deep fascia to the extent that any attempt the patient may make to move the needled region imparts mechanical forces to the needle that may on occasion bend or even make it so misshapen that it is difficult to remove.

While practising superficial acupuncture, the author limits the depth of insertion to 4 mm or less – a depth also described by [Ceccherelli et al. \(2001\)](#); however in later work [Ceccherelli et al. \(2002\)](#) employed a 2 mm insertion. [Sandberg \(2004\)](#) pointed out if the needle tip is inserted to a depth of 4 mm, it may reach the subcutaneous layer; therefore such an approach should be called, ‘subcutaneous needle stimulation’. Meanwhile [Baldry \(2002\)](#), who also advocated the superficial approach, employed a needle tip depth of between 5 and 10 mm.

Although such a shallow insertion achieved by tapping it through a guide tube without further manipulation is usually painless, the mere exhibition of a needle can cause vasovagal syncope, and if the needle is about to be sited over the thorax or any other region where the effects of it being inadvertently thrust more deeply are to be greatly feared, the needle is inserted as parallel to the skin as possible.

## **A randomised study comparing superficial acupuncture with placebo**

[Macdonald et al. \(1983\)](#) set out to determine whether or not the noxious stimuli of sterile 30-gauge (0.30 mm diameter) acupuncture needles inserted without rotation or further stimulation superficially into the skin and subcutaneous layers to an approximate depth of 4 mm for short periods of time once a week were significantly more effective than placebo in relieving low back pain in those patients who had a history of a year or more in duration, had already failed to derive sufficient benefit from conventional measures and whose severity of their condition warranted referral from orthopaedic or rheumatological departments to a pain relief clinic.

The placebo was provided by electrodes (in this case EEG) attached to the skin with micropropore in a lattice work at 2 cm intervals overlying tender regions found by palpation; they were connected by wires to an impressive piece of equipment, an eight channel chart recorder standing some 2 m high, covered with dials and lights, whose cooling system made a 'whirring' sound – but which in fact produced no current or any other form of stimulation. This idea of dummy electrodes being employed as a placebo was also suggested by [Melzack \(1975\)](#).

In those who received acupuncture, the needles were inserted superficially into skin at 2 cm intervals overlying abnormally tender regions.

The patients ( $n=17$ ) were divided into two groups beforehand by a stratified random process designed to divide the sexes as equally as possible between the two groups. The first group – six females and three males – received placebo only; while the second – six females and two males – were treated with superficial acupuncture only.

Both groups happened to be comparable in terms of age, duration of pain, mood scores, number of physical signs and severity of pain assessed before treatment by independent observers.

In both groups, the treatments were repeated weekly in a course of treatments. Each patient was told the first treatment was expected to give only a few hours' relief, but it was hoped that successively prolonged pain relief would follow each treatment given at weekly intervals until a sustained relief of pain was achieved. The maximum number of treatments between the two assessments was arbitrarily set at 10. The number of treatments was reduced, however, if improvement failed to occur or indeed if pain continued to progress. Those who were about to receive placebo surface electrodes were told this was a needle-free treatment coupled to electrical stimulation of such high frequency that it could not be felt.

Subjective measures included a horizontal visual analogue score (0, no pain; 10, pain as bad as it could be) – this was completed on each of seven evenings before each treatment. In addition, on the night before each treatment the same scoring system was used for each of the following activities – walking on level ground, standing still, sitting on a hard chair, rising from a chair, getting out of a bath, turning in bed, putting on socks or stockings, lifting weights, climbing stairs and bending to touch knees.

In terms of objective observations, during examination before a course of treatment and again at its completion, independent examiners recorded whether or not the following signs were present: scoliosis, pelvic tilt, pain on movements of hip, crossed leg pain, femoral stretch test, sensory or motor deficits and reflex changes, loss of lordosis, and impairment in gait, spinal mobility and straight leg raising. They also recorded the severity of pain that they felt the patient was suffering

in terms of (1) ‘minimal’, (2) ‘moderate’ and (3) ‘severe’. Finally they recorded the areas indicated by the patient as being painful on a body outline chart.

One of the main drawbacks encountered in this study was that it was single – rather than double-blind – not only because the practitioner (the present author) could not help knowing which treatment was which but also it was impossible to make sure patients did not describe the method of treatment they had received during their second assessment by the independent observer. However, at that time no one had any idea whether superficial acupuncture carried out in this way was a placebo or not, and every effort was made to retain as unbiased an attitude as possible to see how its effects compared with a placebo.

Bearing this in mind, the results of this investigation, summarised in [Table 9.1](#), showed unequivocal strong support for a beneficial effect of superficial acupuncture as compared with placebo in reducing an overall mean of five measures of chronic back pain severity. In every case, the superficial acupuncture group’s reduction was greater than that of the placebo group, and the differences between the two groups were all with one exception statistically significant when tested by Wilcoxon rank-sum tests.

The authors concluded it is not always necessary to insert a needle into deep structures but merely into skin overlying abnormally tender regions to achieve significant overall benefit in these measures of chronic low back pain ( $p < 0.01$ ) as compared with placebo.

## Superficial vs. deep needling

Less neuronal stimulation occurs when a needle is inserted into skin alone without further manipulation as compared with a needle tip traversing skin and entering the deep tissues in the same location and then rotated back and forth and manipulated up and down in a quest for *de qi* ([Chae et al., 2011](#)). Furthermore plastic changes within the central nervous system are more likely to occur and last longer when noxious stimulation is applied to deep as compared with superficial tissues ([Sluka, 2002](#)). Yet some well-conducted studies show there is no significant difference when the effects of shallow needling are compared with deep in the same needle sites, for example [Näslund et al. \(2002\)](#) in a study of the relief of idiopathic knee pain and [Ceccherelli et al. \(1998\)](#) in the reduction of inflammation induced in a rat by capsaicin.

Many of the unresolved difficulties in interpreting sham interventions in acupuncture trials have been reviewed ([Dincer and Linde, 2003](#); [Lund et al., 2009](#); [Lundeberg et al., 2011](#); [Zhang et al., 2010b](#)). The importance of all of this is considered by [Lundeberg et al. \(2008\)](#) who declared if at least on some occasions superficial needling has an effect, it can no longer always be considered ‘sham’; if that is so, some of the scepticism produced by trials that fail to show a significant difference between the effects of deep and superficial needling employed as a ‘control’ might be allayed.

## The non-placebo effect of skin stimulation

Hypoalgesia has been achieved by stimulating skin overlying tender regions in several ways: for example by employing superficially applied counter-irritants ([Melzack et al., 1977](#)) and cooling the skin with ethyl chloride spray ([Travell, 1952](#)). The Chinese themselves often confine stimulation to the skin when they apply heat via moxa cones, elicit haematomata by cupping or when they employ very short (plum blossom) needles.

Could the effects of all of this cutaneous stimulation be placebo, when we take stock of the idea: *‘A placebo effect is a genuine psychological or physiological effect, in a human or an animal, which is attributable to receiving a substance or undergoing a procedure, but is not due to inherent powers of that substance or procedure?’* ([Stewart-Williams and Podd, 2004](#))

TABLE 9.1 ■ Results of a single blind randomised study of superficial acupuncture compared with placebo (Macdonald et al., 1983)

<i>Patient groups</i>	<i>Mean percentage reductions</i>					
	<b>Pain relief after each treatment (%)</b>	<b>Pain score reduction (%)</b>	<b>Activity pain score reduction (%)</b>	<b>Physical signs reduction (%)</b>	<b>Severity and pain area reduction (%)</b>	<b>Combined average reduction (%)</b>
Acupuncture, <i>n</i> =8	77.35	57.15	52.04	96.78	73.75	71.41
Placebo, <i>n</i> =9	30.14	22.74	5.83	29.17	18.86	21.35
Significance of difference <sup>a</sup>	<i>p</i> <0.01	NS	<i>p</i> <0.05	<i>p</i> <0.01	<i>p</i> <0.01	<i>p</i> <0.01

<sup>a</sup>Significance assessed by the Wilcoxon rank-sum test.

When we consider the power and variety of responses to noxious stimulation not only within the skin itself but also in the central nervous system, the idea that superficial acupuncture is devoid of ‘inherent powers’ that might alter the balance of pain processing is dashed aside.

## Nature of cutaneous neuronal responses

Skin is composed of three coats: the outer stratum corneum; an intermediate layer, the epidermis; and the innermost one of all, the dermis. Components of the epidermis include immune cells such as keratinocytes, melanocytes and Langerhans cells.

The epidermis is endowed with a three-dimensional network of un-myelinated C-fibres whose branches contact not only Langerhans and Merkel cells but also keratinocytes and melanocytes (Roosterman et al., 2006). Merkel cells are effectively mechano-receptor ‘plates’ slung between keratinocytes. These are excited whenever there is inward displacement of the skin, particularly when shear forces are employed or the skin is indented in one small place (Halata et al., 2003). Merkel cells are in contact not only with C-fibres, but also A $\delta$  and A $\beta$  fibres – each type of fibre forming its own dense syncytium at the dermoepidermal junction. Thus a Merkel cell is ideally qualified as a ‘multifunctional nerve end organ’ to sense external stimuli (Reinisch and Tschachler, 2005).

In good health, few if any neuromediator substances can be detected in the skin. Following noxious stimulation of the skin, however, epidermal innervation produces an array of regulatory neuropeptides, neurotrophins, neurotransmitters and nitric oxide (Carlsson et al., 2006; O’Sullivan et al., 1998; Roosterman et al., 2006; Tachibana and Nawa, 2005). As far as the role of nitric oxide is concerned, primary afferent nociceptors are equipped with a phenomenon that has been explored by Sergio Ferreira’s team who call it a telephenomenon: nitric oxide diffuses throughout the neuron so rapidly from the periphery that it can alter the behaviour of the central axon lying within the central nervous system almost simultaneously – such a rapid signalling occurs in both directions from one end of the nociceptive neuron to the other (Funez et al., 2008). Thus cutaneous nerves ‘converse’ in afferent and efferent directions with higher centres via dorsal root ganglia and coordinate reactions to external threat.

## Neurogenic inflammation

Within a few seconds of inserting a needle, the behaviour of the neuronal network leads to a reddening of the skin, caused by vasodilatation in precapillary arterioles. Indeed an increase in cutaneous blood flow following acupuncture was recorded by Jansen et al. (1989) and described by Carlsson et al. (2006).

Although it does not involve central synapses, Bruce (1913) and Lewis (1936) described this phenomenon as an ‘axon reflex’ – a reaction of afferent terminals to noxious stimulation that release vasoactive and pro-inflammatory neuropeptides. The skin’s ability to perform this way turns it into a ‘peripheral lens’ that not only observes but reacts to physical stimuli before they are processed centrally (Le Bars, 2002). Jansc  et al. (1967) had another term for these phenomena, ‘Neurogenic inflammation’.

There is a balance between pro- and anti-inflammatory substances produced in the skin. There is for example an endogenous counter-regulation of inflammation called the ‘sensocrine’ function of cutaneous sensory nerve endings by Helyes et al. (2004). Here anti-inflammatory substances such as galanin, vasoactive intestinal peptide, pituitary adenylate cyclase-activating polypeptide and somatostatin are released from activated sensory nerve terminals. Whereas the spinal cord and mid-brain structures are required for many acupunctural effects, needling skin may produce local analgesic anti-inflammatory effects without central intervention. For example, an anti-inflammatory agent, adenosine, is released in tissues that have been needled (Goldman et al., 2010). In addition, acupuncture stimulation releases two analgesic neuropeptides that can

modulate the immune system by inhibiting the release of pro-inflammatory neuropeptides from monocytes and macrophages: somatostatin (Dong et al., 2005) and the endocannabinoid anandamide (Chen et al., 2009).

## Monitoring local circulation

One of the easiest ways to estimate the area of the surface markings of an axon flare responses is to use photography (Nischik and Forster, 1997). The colour intensity of a digital photograph can be adjusted digitally to determine the extent of the flare reaction.

When a needle on its own (in this case a 25 Gauge hypodermic gauge) is inserted to a depth of 10 mm into an un-inflamed region without injecting any substance or being subjected to manual or electrical stimulation, changes in blood flow occur. Rayman et al. (1986) were the first to record changes in microvascular flow in the superficial tissues in its immediate vicinity by means of laser Doppler flowmetry. Here they compared differences in the reactions of normal subjects as compared with those with Type 1 diabetes. In normal subjects, within 15 min of needle insertion, a hyperaemia occurs: the local cutaneous blood flow is increased to 20 times the resting state. It gradually subsides back to baseline over the next 2–3 days. These responses are significantly less pronounced in those suffering Type 1 diabetes.

Another approach employing not only a photodetector but also infra-red and green LEDs is called photoplethysmography: its optical geometry is such that it monitors blood flow not only in the skin but also in underlying muscles (Allen, 2007; Hagblad et al., 2010). Photoplethysmography has been used in a series of studies to compare the effects of (1) deep needling, where one needle was employed with (2) superficial needling, where three needles were inserted. In one study, Sandberg et al. (2005) compared the effects of local deep and superficial needling on the blood flow in trapezius muscle and the skin overlying it in three groups: (1) healthy subjects, (2) patients diagnosed as having chronic work related ‘myalgia’ where tenderness was localised to the trapezius region on one side of the body only and (3) those suffering fibromyalgia, presenting with chronic bilateral pain in many regions. They observed an increased blood flow in both skin and muscle in all three groups whether deep or superficial needling was employed. However the least increase in skin and muscle blood flow occurred in the myalgia group. The greatest change as far as muscle blood flow was concerned occurred in healthy subjects when they received deep needling. In healthy subjects superficial needling produced less increase in muscle blood flow than deep needling, while in fibromyalgia patients superficial needling was as effective if not more so in producing increased muscle blood flow.

## Hypothesis that may explain superficial needling

Why should needling skin reduce tenderness arising from tissues lying beneath it? As yet there is no answer. However a hypothetical answer can be provided. This is the ‘flexor withdrawal reflex’ – a highly organised central neuronal response to noxious stimulation studied since the days of Sherrington.

Stimulating one region, even if only minimally and cutaneously with a needle, is likely to have a profound effect on the behaviour of muscle tone in many regions, in particular the muscle region immediately beneath the needled site, in such a way that the needled portion of the body is withdrawn and can in this way ‘escape’.

There are multireceptive neurones within the spinal dorsal horn that receive inputs from deep structures such as muscles but nevertheless have cutaneous receptive fields whose boundaries not only fluctuate but are often placed in a region distal to the muscle (Le Bars, 2002).

The function of all of this is to orchestrate appropriate contraction and relaxation of muscles so a portion of the body escapes noxious stimulation.

Andersen (2007) stimulated skin on the anteromedial aspect of the foot in man and observed the withdrawal response. Here tibialis anterior became excited in an attempt to escape via dorsiflexion.

Stimulating the heel region, however, caused excitation of a different muscle, the medial head of gastrocnemius; this tends to cause withdrawal via plantarflexion.

One can not help observe that referred pains from gastrocnemius and tibialis anterior reside distally in such regions as the foot (Travell and Simons, 1983). Is it possible receptive fields also play a part in the phenomenon of 'referred pain'?

When a patient who on palpation is found to have an abnormally tender region in the gastrocnemius muscle says, 'I have pain in my heel', what he does not say is that any attempt to dorsiflex the foot or put any weight on his heel increases fascial mechano-receptor activity in the gastrocnemius muscle. In this case, noxious stimulation applied to the plantar region of the foot may make the pain worse – as such stimulation is expected to increase neural activity associated with the gastrocnemius muscle region.

However, if stimulation is applied in a lattice of needles inserted superficially into the skin overlying the surface markings of the abnormally tender portion of gastrocnemius itself, this produces benefit as it tends to induce a withdrawal reflex where extensors of the knee are stimulated and gastrocnemius muscle activity is inhibited – all of this to allow the needled region to escape – so much so the patient can now resume a more normal gait for as long as these effects last.

## Japanese tradition of superficial acupuncture

Little in this world is new. The Japanese have been practising superficial acupuncture for centuries (Kawakita et al., 2006).

Kobayashi et al. (2010) described the practice of acupuncture arriving from Korea in the sixth century AD. From 1635, outside influence was banned for two centuries. As a result, some 30 different types of acupuncture evolved. In many traditions, the location of the needle is determined by sensations arising from the practitioner's finger tips when 'troubled spots' on the patient's body are palpated.

In 1680, the father of Japanese acupuncture, Sugiyama Waichi, who became blind at the age of 10, asked the Goddess to explain to him how to insert a needle painlessly. He fasted for several days. On leaving the Temple, he fell over a large stone. When recovering consciousness, he found the answer – under his hand was a piece of bamboo inside which there was a pine needle. Thus he discovered the first guide tube. This tube placed around a needle prevents needles from buckling or bending too far when inserted rapidly into the skin by merely tapping the handle downwards without 'twirling' and allows the insertion of very 'thin' needles that are favoured by the Japanese: these range in diameter from 0.12 to 0.18 mm.

In some traditions, the needle tip may only be allowed to make contact with the outermost layer of skin. On the other hand, it may be inserted 'super-superficially' to a depth of 1 mm or less or perhaps a little more allowing the needle tip to reach depths of 1–5 mm.

Dann (2007) declared, '*The most skilful healer treats the surface hairs ... The healer next in skill treats the subcutaneous tissues ... the healer next in skill after that treats the sinews and the vessels ...*'

Just touching the skin or inserting the needle superficially is often not felt at all by a patient in pain. This is particularly useful in treating infants, nervous adults and the elderly, and as declared by Kodo Fukushima in the 1950s, '*It may treat a sleeping cat*'.

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## Auricular acupuncture

T.I. Usichenko ■ E.F. Anders

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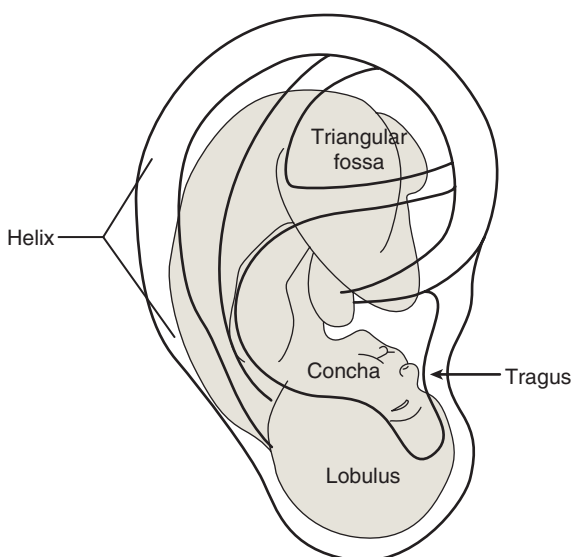
## Introduction

Auricular acupuncture (AA, often called also auriculotherapy) is a complementary medicine technique originally based on a hypothesis that the entire human body is represented on the external auricle (Fig. 10.1). It is postulated that the pathology of the organs of the human body leads to changes of the respective areas of the external auricle. These changes can be identified as areas with tenderness and reduced tissue density on palpation and reduced electrodermal resistance (EDR). Stimulation of the areas, connected to an organ with 'pathology' is believed to improve the function of the organ or relieve the concomitant pain. The representation of the human body on the pinna is often called somatotopic, analogous to motor and sensory somatotopy in human cortex, described by Penfield and Rasmussen (1950) on the basis of experimental research. Thus AA is based rather on the theory of reflexotherapy than on the traditional Chinese system of energy circulation along the meridians.

AA is commonly used in treatment of diseases, mainly affecting the central nervous system, such as treatment of acute and chronic pain, and psychiatric disorders including substance abuse. Almost all modes of stimulation are used for auriculotherapy, including needling, acupressure and electrical stimulation. The most commonly used technique (in comparison with body acupuncture) is the insertion of semipermanent press needles, which are left *in situ* for several days and even weeks and can be stimulated by the means of massage by the patients themselves.

## History

Rudimentary forms of auricular stimulation were reported by historians and archaeologists to be present in almost all ancient cultures (Gori and Firenzuoli, 2007). Also, the practice of cauterising a part



**Figure 10.1** The hypothesised representation of the whole human body as an inverted embryo on the auricle.

of the auricle was common among certain tribes in Arabia as long as 3000 years ago. In ancient Egypt the women pricked the external auricles with a needle or cauterised with heat for contraceptive purposes. Mediterranean sailors wore earrings through the centre of ear lobule in order to improve vision. Ancient Greek physicians made small openings in the retroauricular veins to treat ejaculation problems. The physicians in ancient Persia treated sciatic pains and sexually related diseases by cauterization of the external auricle. Later in Europe, the Italian anatomist and surgeon Antonio Valsalva published his famous *Tractatus de Aure Humana*, where he described the treatment of toothache by scarification of the antitragus (Valsalva, 1704). The French *Journal des connaissances medico-chirurgicales* in 1850 reported a case series of 13 patients with sciatic pain treated by cauterization with a hot iron applied to external auricle (Gori and Firenzuoli, 2007). All but one patients improved completely.

According to ancient sources of Traditional Chinese Medicine, several acupuncture meridians are connected to the external auricle; the organ Heart had direct 'energetic' connection to the ears (Herget, 1998). Ancient Chinese physicians distinguished certain somatotopy of the auricle: the tragus corresponded to nasopharynx and the lungs, the concha represented the heart and the spleen, the helix was attributed to liver.

However, in its most highly differentiated form (with more than 100 auricular points), auriculotherapy was described by French physician Paul Nogier, who is often called 'The Father' of AA. Nogier observed the relief of low-back pain in his patients after cauterization of certain sites on the external auricle, performed by lay healers. He replaced the hot iron with needles, and for this and other indications achieved considerable clinical success. Based on his own observations, Nogier postulated that the pathology of the organs of human body leads to changes of the respective areas of the external auricle and proposed the somatotopic concept of an inverted foetus map on the external auricle; see Figure 10.1 (Nogier, 1957). The findings of Nogier were published in *German Journal of Acupuncture* in 1957, which had an international circulation. Thus, after learning about the somatotopic auricular map of Nogier, Nanjing Army Ear Acupuncture Research Group from China verified the clinical effectiveness of auricular somatotopy in a study with more than 2000 patients, recording which ear points corresponded to specific diseases (Huang, 1974). The results seemed to confirm the somatotopic map of the auricle proposed by Nogier.

Later Terry Oleson from the University of California evaluated the claimed somatotopy of the ear in a double-blinded experimental investigation. He examined the skin conductivity and tenderness of the ears in 40 patients with musculoskeletal pain. The concordance between the established medical diagnosis and the auricular diagnoses was 75%, apparently confirming the findings and somatotopic map concept of Nogier ([Oleson et al., 1980](#)).

## Mechanisms of action

Although AA is widely used as a complementary treatment for a variety of painful and psychiatric disorders, the therapeutic mechanisms of AA remain unknown, and the somatotopic map is subjected to scepticism ([Ernst, 2007](#)). At the present time, no neuroanatomical pathways are known to connect the ‘diseased’ body organs with the external auricle and explain the clinical effects of AA.

Several experimental investigations confirmed the functional connections of viscera and auricular skin. So, the EDR of the ears in rats decreases after induction of experimental peritonitis immediately following surgery, persists for 7–14 days and returns to the control level when the healing is almost complete ([Kawakita et al., 1991](#)). In another investigation, [Ceccherelli et al. \(1999\)](#) induced neurogenic inflammation by injecting capsaicin into the paw of rats and observed the appearance of the area with a lower electrical skin resistance on the external auricle. Percutaneous electrical stimulation applied to these ear points bilaterally, but not the stimulation of auricular sham points, led to a reduction of inflammatory oedema of the paw and to analgesia.

### Clinical points

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Little evidence supports somatotopic representation in the ear, but some evidence supports a link between changes in auricular skin and the viscera.

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In another animal experiment, the stimulation of the area corresponding to acupuncture point MA-IC1 (lung) elicited the most pronounced decrease in blood pressure and heart rate and increase of gastric pressure in comparison to stimulation of other areas, receiving innervation from other sources ([Gao et al., 2008](#)). This effect was abolished by blockade of vagal transmission with intravenous injection of the muscarinic receptor blocker atropine. Stimulation of the acupuncture point MA-IC (heart) led to decrease of arterial pressure and heart rate, which was accompanied by the activation of cardiac-related neurons of the nucleus tractus solitarius. Again, this reaction was attenuated by the administration of atropine ([Gao et al., 2011](#)). These results do not support the theory of a highly specific ‘somatotopic’ map of the auricle but help to elucidate the neurophysiological mechanisms of AA.

Measuring blood oxygenation level dependant (BOLD) response of the brain to electrical stimulation of concha in healthy volunteers, [Dietrich et al. \(2008\)](#) observed the activation of the locus coeruleus, thalamus, insula and some other higher order relay nuclei of vagal afferent pathways. Another fMRI investigation confirmed the previous results showing the increased BOLD signal in the insula, precentral gyrus and the thalamus under electrical stimulation of auricular concha ([Kraus et al., 2007](#)). Moreover, BOLD signal decreases were seen in limbic brain areas, including the amygdala, hippocampus, parahippocampal gyrus and the middle and superior temporal gyrus. Earlobe stimulation as a sham control intervention did not show similar effects.

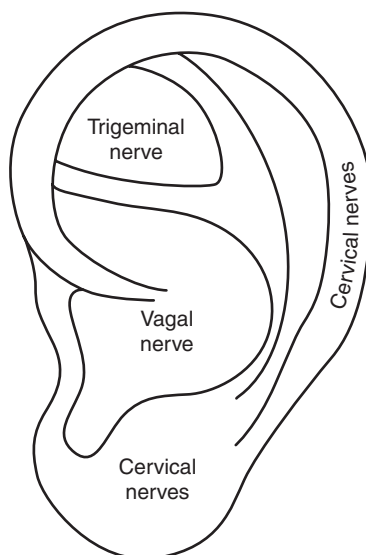
### Clinical points

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Auricular stimulation activates brainstem nuclei and limbic system.

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The observed effects are supported by the data from neuroanatomy and physiology. The concha and triangular fossa of the pinna receive an overlapping nerve supply by cranial



**Figure 10.2** Nerve supply of the external auricle according to [Peuker and Filler \(2002\)](#).

(trigeminal and vagal) nerves ([Fig. 10.2](#)), whereas the peripheral regions of the auricle – helix and scapha – are innervated by spinal C1–C3 nerves ([Peuker and Filler, 2002](#); [Williams et al., 1989](#)). The afferent fibres of the auricular branch of the vagal nerve, as shown by using the transganglionic tracing method of horseradish peroxidase, terminate in the brain stem nuclei (mainly in the ipsilateral nucleus solitarius, principal sensory and spinal trigeminal nuclei, area postrema and cuneate nucleus) ([Nomura and Mizuno, 1984](#); [Satomi and Takahashi, 1991](#)). It is well known that the solitarius and spinal trigeminal nuclei are involved in the transmission and processing of visceral nociceptive stimulation, whereas the analgesic effect of vagal stimulation is mediated through nucleus tractus solitarii including the system of endogenous opioids ([Aicher and Randich, 1988](#); [Randich et al., 1988](#)). In chronic pain patients, electrical stimulation of auricular points led to pain relief and was associated with increased beta-endorphin in cerebral fluid ([Clement-Jones et al., 1980](#)).

### Clinical points

Concha and triangular fossa are innervated by cranial nerves; helix and other peripheral regions of the auricle are innervated by cervical nerves.

Beyond such exotic techniques as AA, vagal nerve stimulation (VNS) is an FDA-approved therapy for the adjunctive treatment of epilepsy and medication-resistant major depression ([George et al., 2007](#)). VNS is currently being investigated in clinical studies as a potential treatment for essential tremor, sleep disorders, cognitive deficits in Alzheimer's disease, anxiety disorders, obesity and pain ([Groves and Brown, 2005](#)). VNS appears to affect pain perception in depressed adults; a possible role of VNS in the treatment of severe refractory headache, intractable chronic migraine and cluster headache has also been suggested ([Multon and Schoenen, 2005](#)). The stimulation of the vagus nerve alone leads directly to clinically significant pain reduction ([Kirchner et al., 2000](#)).

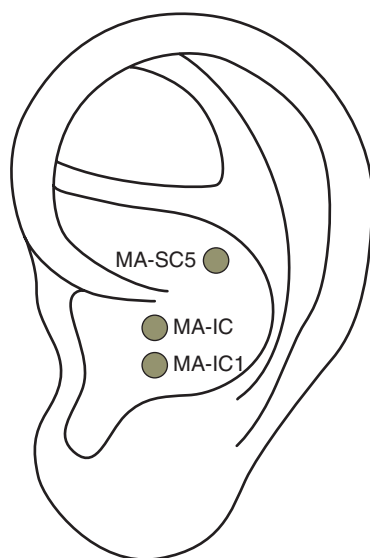
Regarding the anatomy of neural pathways from the external auricle, the physiological effects of its stimulation in addition to clinical data, it can be suggested that the mechanism of AA can be explained at least by stimulation of cranial nerves with subsequent activation of several nuclei in the brainstem.

## Nomenclature of AA

There are several nomenclature systems for AA. The two most frequently used systems are the Nogier nomenclature system and World Health Organization (WHO) nomenclature. Nogier initially described his nomenclature using the names of ‘corresponding’ organs and organ systems and added numbers to them later (Nogier, 1977). The point lung, for example, received the number 101, point Shenmen received number 51, etc., according to that system. During the international meeting of the experts in Seoul, the WHO nomenclature was proposed as the international standard (WHO, 1987). For example, the lung point is identified as MA-IC1, Shenmen point as MA-TF1 according to international WHO nomenclature. The latter nomenclature uses only 43 points or zones, which are not enough to cover all empirically ‘discovered’ points of AA. Because of this, the Nogier nomenclature is still used more frequently in clinical practice. In the chapter we characterise the points according to standard WHO nomenclature and give corresponding names according to Nogier nomenclature in parentheses.

## Auricular diagnosis

Usually auricular diagnosis is established before the start of auriculotherapy. This means that the points (or areas) of the external auricle, which are going to be stimulated during the therapy will be identified, using such methods as (1) inspection, (2) palpation and (3) measurement of EDR. During inspection the changes of skin colour, presence of papules, appearance of capillary and desquamation at the sites of acupuncture points/zones are registered. In 20 patients with liver dysfunction, the zone MA-SC5 (liver, Fig. 10.3) revealed at least one of the skin signs described earlier, with a prevalence 74% which was higher than 24% in 25 healthy control subjects (Cheing et al., 2009). The examination of the tenderness of auricular points, introduced by Nogier, is also widely used in clinical practice. This method was verified by Oleson et al., 1980 in patients with



**Figure 10.3** Point MA-SC5 (liver) was frequently identified in patients with liver dysfunction in the study of Cheing et al. (2009). Acupuncture points MA-IC (heart) and MA-IC1 (lung) were identified as the areas of lower electrical skin resistance in patients with coronary artery disease and but not in healthy subjects (Saku et al., 1993).

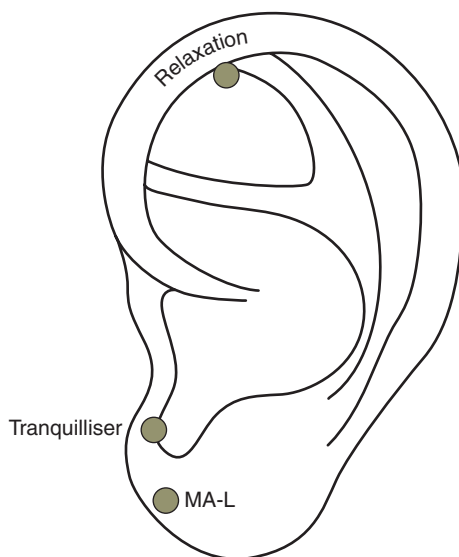
musculoskeletal pain as described earlier. Electrodermal measurements are the most objective method that can be used for detection of AA points. [Saku et al. \(1993\)](#) studied the changes of EDR of the external auricle in patients with coronary artery disease and in healthy subjects. The authors observed the areas of low EDR in the centre of concha auriculae, the zone representing the heart and lung systems in the empirical model of AA (see [Fig. 10.3](#)). The frequency of the points with low EDR in the centre of concha was highest among patients with acute myocardial infarction (MI); patients with old MI and angina pectoris also revealed the higher incidence of low EDR points in comparison to healthy subjects. [Romoli et al. \(2010\)](#) studied tender areas with reduced EDR on the auricles of 78 patients before and after elective hysteroscopy. They found that the auricular areas that were rich in tender points with lower EDR overlapped with historical, empirically defined, Chinese and French 'somatotopic' representation of the uterus on the external auricle. The number of points identified was significantly higher after hysteroscopy.

## Anaesthesia and pain therapy

In clinical anaesthesia, auricular stimulation has been reported to treat preoperative anxiety, reduce intraoperative anaesthetic and analgesic requirement and relieve acute postoperative pain.

### PREOPERATIVE ANXIETY

Auricular stimulation using indwelling semipermanent AA needles as well as acupressure with attached seeds and metal balls is used to reduce situational anxiety before surgery. In one recent investigation on the anxiolytic effect of AA this intervention was compared to sham acupuncture and non-intervention control group in 182 patients scheduled to undergo dental procedures ([Michalek-Sauberer et al., 2012](#)). The AA points used for stimulation in this study were MA-L (master cerebral), tranquilliser point and relaxation point ([Fig. 10.4](#)). AA reduced state anxiety (measured using the Spielberger State Trait Anxiety Inventory) more effectively than sham acupuncture and non-intervention control.



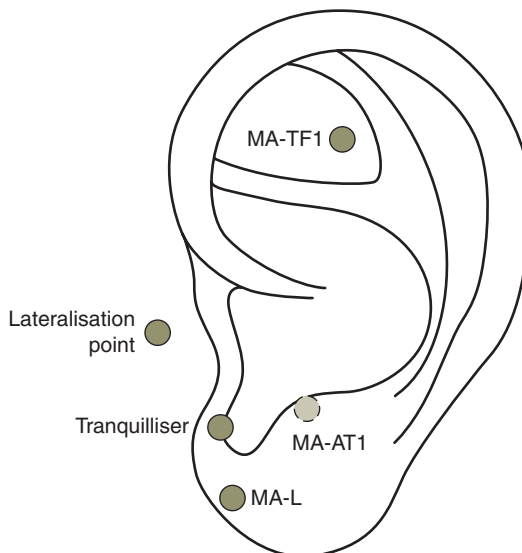
**Figure 10.4** Points MA-L (master cerebral), tranquilliser and relaxation point used to treat preoperative anxiety procedures ([Michalek-Sauberer et al., 2012](#)).

More interesting for clinicians is the possibility that auricular stimulation could replace benzodiazepines, which are still widely used in Europe to treat preoperative anxiety within standard premedication before surgery. Already in 1987 Lewis and Litt compared oral diazepam with auricular acupressure using silver balls (applied to MA-L point) and standard psychological relaxation technique in 90 patients scheduled to surgery under general anaesthesia. Auricular acupressure and relaxation method were as effective as diazepam for premedication and in certain respects had advantages over this drug: acupressure patients had less palmar sweating, reported fewer side effects of diazepam (oversedation, dysphoria) and better satisfaction with treatment (Lewis and Litt, 1987). Later, Karst et al. (2007) confirmed these results using the same model of situational anxiety in 67 patients, scheduled for dental extractions. The authors compared AA (applied to the points MA-L, tranquilliser point and relaxation) with intranasal midazolam, placebo acupuncture and no treatment. The patients from the AA group and the midazolam group were less anxious as compared with patients in the placebo acupuncture group and non-intervention group. Patient compliance assessed by the dentist was significantly improved if AA or application of intranasal midazolam had been performed.

### INTRAOPERATIVE DRUG REQUIREMENT

Two excellent experimental investigations demonstrated that auricular stimulation can reduce the dose of volatile anaesthetic desflurane required to prevent the movement of extremities in response to noxious electrical stimulation in healthy volunteers. In one of these studies the acupuncture needles were applied to the points MA-TF1 (Shenmen), MA-AT1 (thalamus), tranquilliser and MA-L (master cerebral) on the right ear (Fig. 10.5). On another day the volunteers were anaesthetised without acupuncture (Taguchi et al., 2002). On the day without acupuncture the volunteers required more desflurane to prevent movement than on the acupuncture day: desflurane concentration 4.9 (0.7; SD) versus 4.4 (0.8) vol.% ( $P=0.003$ ).

Greif et al. (2002) used electrical stimulation applied bilaterally to the lateralisation control point, situated 3 cm anterior to the top of the tragus. The 10-mA current was set to 299 Hz on the



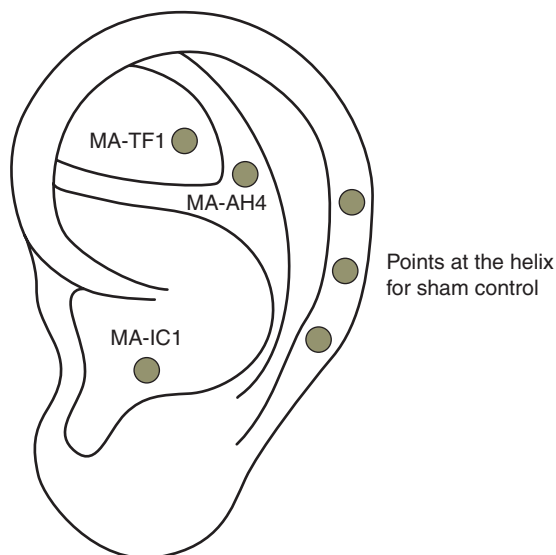
**Figure 10.5** Points MA-TF1 (Shenmen), MA-AT1 (thalamus), tranquilliser, MA-L (master cerebral) and lateralisation control point used to reduce the anaesthetic requirement in healthy volunteers in experimental setting (Taguchi et al., 2002; Greif et al., 2002).

dominant side of the face and to 149 Hz on the contralateral side. The effect was compared with no stimulation in a crossover design. Electrical stimulation of the lateralization control point in 20 healthy volunteers reduced anaesthetic requirement by 11% ( $P < 0.0001$ ).

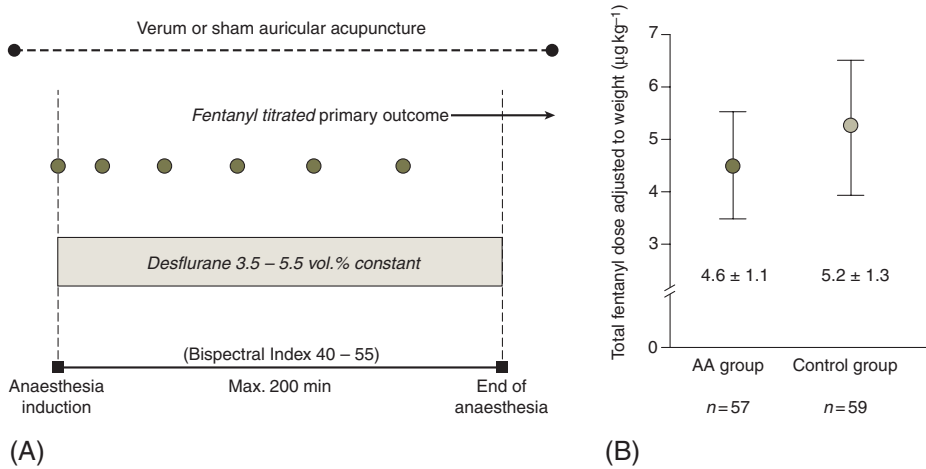
Wetzel et al. (2011) studied intraoperative analgesic requirement in patients during total hip arthroplasty (THA) under AA. The patients were randomly assigned to needling of auricular points MA-TF1 (Shenmen), MA-AH4 (hip) and MA-IC1 (lung) or a sham procedure (Fig. 10.6). Fixed indwelling needles were placed ipsilateral to the surgery site. The patients received general anaesthesia with desflurane, with end-tidal concentration kept constant within 3.5–5.5 vol.% to maintain the depth of general anaesthesia at a constant level, measured using Bispectral Index monitoring, kept between 40% and 55% (Fig. 10.7). The anaesthesiologists were asked to titrate fentanyl to keep the heart rate and blood pressure within 20% of baseline values. The primary outcome was fentanyl amount given during surgery. The patients and anaesthesiologists were unaware of group allocation. The success of patients' and anaesthesiologist blinding was also documented in this study. The data of fentanyl requirement in 116 patients were available for the final analysis. Patients from AA group required 15% less fentanyl during surgery than the controls; this difference was statistically significant but without clinical relevance.

## DOSE REQUIREMENT FOR LOCAL ANAESTHETICS

Kindberg et al. (2009) compared ear acupuncture directly to local anaesthesia (LA) as a sole pain relief procedure in women, who required postpartal surgical repair. The midwives received a 2-h hands-on course on administering ear acupuncture for perineal pain relief. A total of 207 women were randomised to receive ear acupuncture (105) and local anaesthetics (102), respectively. Women who received AA reported more pain than the LA group (3.5 vs. 1.5;  $P < 0.01$ ), required more additional analgesics and were less satisfied with the pain relief method. So, AA alone was inferior to LA in relief of pain during perineal repair.



**Figure 10.6** Auricular points MA-TF1 (Shenmen), MA-AH4 (hip) and MA-IC1 (lung), used for complementary analgesia in anaesthetised patients during total hip arthroplasty. The points on the helix were used for sham control procedure.



**Figure 10.7** (A) Schema of standardised general anaesthesia from the study of [Wetzel et al. \(2011\)](#). General anaesthesia was performed using volatile anaesthetic desflurane; the depth of anaesthesia was measured using Bispectral Index. The fentanyl was titrated to prevent movements during surgery and to ensure that the heart rate and mean arterial pressure were within 20% of baseline values. (B) Total amount of intraoperative fentanyl, adjusted to body weight given as mean  $\pm$  SD in microgram per kilogram body mass;  $P=0.008$ , Student's  $t$ -test.

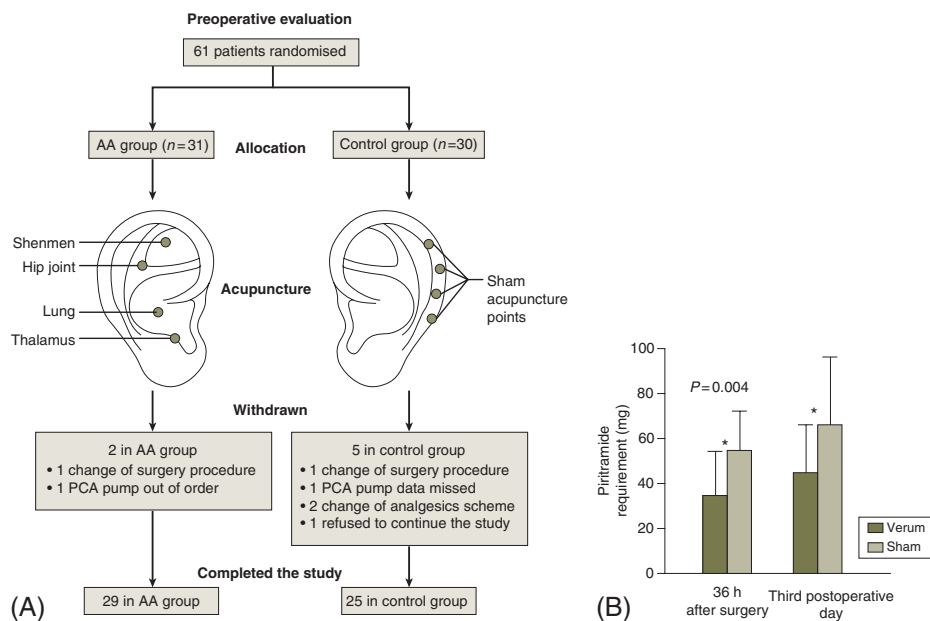
## ACUTE POSTOPERATIVE PAIN

Two systematic reviews of randomised controlled trials (RCTs) comparing auricular stimulation to sham, placebo or standard therapy in treatment of pain suggested that this therapeutic modality may be effective for treatment of postoperative pain ([Usichenko et al., 2008](#); [Asher et al., 2010](#)). One of them, which focused on the efficacy of AA for postoperative pain control, found that eight out of nine included RCTs showed that AA was superior to a variety of control conditions ([Usichenko et al., 2008](#)). The heterogeneity of the outcome measures in the studies included in the review (pain intensity, postoperative analgesic requirement or both) precluded the pooling of data in meta-analysis.

One of the parameters which could have been influenced by AA in the postoperative period is the requirement of analgesics used to treat postoperative pain. So in one typical investigation, included in the review, AA with indwelling fixed needles was used to treat acute postoperative pain in patients after THA ([Usichenko et al. 2005a,b](#)). The patients were randomly allocated to receive AA or sham procedure. For acupuncture the points MA-TF1 (Shenmen), MA-AH4 (hip), MA-IC1 (lung) and MA-AT1 (thalamus) were used ([Fig. 10.8A](#)). Four non-acupuncture points on the auricular helix were used as an invasive sham procedure. Permanent press AA needles were retained *in situ* 3 days after surgery. Postoperative pain was treated with intravenous piritramide (opioid receptor agonist with analgesic potency of 0.7 compared with morphine) using a patient-controlled analgesia (PCA) pump. The amount of postoperative piritramide via PCA was used to evaluate postoperative analgesia. Fifty-four patients (29 AA and 25 controls) completed the study. They were sufficiently blinded to the group allocation: differences between the groups regarding patients' opinion concerning success of blinding were not significant. AA reduced piritramide requirement by 36% ( $P=0.004$ ; see [Fig. 10.8B](#)). This effect was not only statistically significant but might have an impact on clinical practice.

## Clinical points

Evidence from RCTs demonstrates an opioid-sparing effect of AA for postoperative pain.



**Figure 10.8** (A) Flow diagram of the study from Usichenko et al. (2005a,b). For acupuncture the points MA-TF1 (Shenmen), MA-AH4 (hip), MA-IC1 (lung) and MA-AT1 (thalamus) were used for postoperative pain control after total hip arthroplasty. Four non-acupuncture points on the auricular helix were taken for invasive sham control procedure. (B) Main result of the study: postoperative pir tramide requirement given as mean and standard deviation 36 and 72 h after surgery PCA, patient controlled analgesia.

Fifteen RCTs on auricular stimulation for postoperative pain treatment are available (Table 10.1). Only two of these show no benefit of auricular stimulation for that indication, and one of these, reported by Holzer et al. (2011) in 40 patients after laparoscopic gynaecological surgery, revealed several flaws in design (White, 2011). In a typical investigation, He et al. (2013) studied the effect of auricular acupressure on postoperative pain in patients after total knee arthroplasty. Ninety patients with degenerative osteoarthritis were randomised into two groups: the acupressure group received embedded *Vaccaria* seeds at four specific points – MA-AH3 (knee joint), MA-TF1 (Shenmen), MA-AT1 (thalamus) and MA-AH7 (sympathetic) ipsilateral to the surgery site. The control group received acupressure at four non-acupuncture points on the auricular helix (Fig. 10.9). The pain scores were lower in the acupressure group at 3, 4, 5 and 7 days after the surgery. Patients in the acupressure group consumed lower doses of analgesic than those in the control group after surgery and reported analgesia-related adverse effects. Moreover, acupressure applied to AA points promoted earlier rehabilitation of the patients.

### Clinical points

Acupuncture's opioid-sparing effect is similar to that of the best non-opioid analgesic drugs.

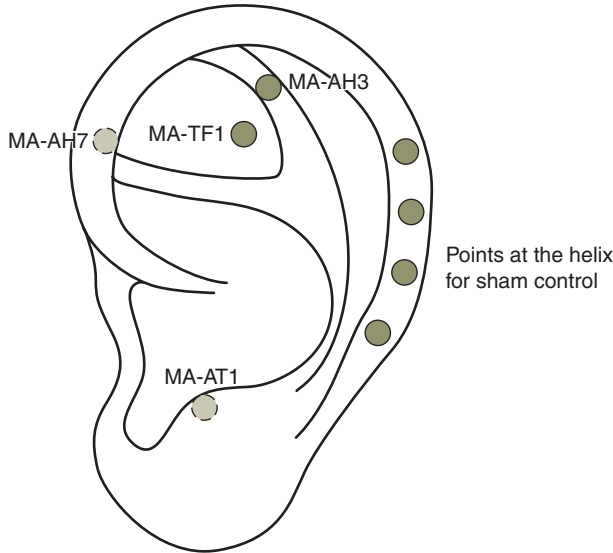
In their systematic review on the effect of auriculotherapy on postoperative analgesic requirement, Asher et al. (2010) calculated the opioid-sparing effect of auricular stimulation in the investigations where postoperative opioids were delivered using PCA pumps. According to their estimation, auricular stimulation reduced opioid requirement by 40%. The size of the opioid-sparing effect of auricular stimulation was larger than the opioid-sparing effect of commonly used analgesic acetaminophen (20%; Remy et al., 2005), and ibuprofen (30%; Singla et al., 2010) and was comparable with that effect of dipyrone (metamizol) (Chaparro et al., 2012) as shown in Table 10.2.

TABLE 10.1 ■ Randomised controlled trials on the effects of auricular acupuncture in treatment of postoperative pain

Reference	Operation	Number of patients	Verum procedure (number of patients)	Control procedure (number of patients)	Primary outcome	Results	Jadad scale
Wang et al. (1988)	Thoracotomy	36	EAA (19)	Standard therapy (17)	Pain intensity Opioid requirement Pulmonary function	EAA better than control for all measured parameters	1
Lewis et al. (1990)	Burns	11	EAA (11)	Placebo pill (11)	Pain intensity	EAA sessions reduced pain intensity	3
Mann (1999)	THA	100	AA (50)	ST (50)	Analgesic requirement Pain intensity	Pain intensity and analgesic requirement decreased in AA versus ST	2
Usichenko et al. (2005a)	AKA	20	AA (11)	SA (9)	Ibuprofen requirement	Ibuprofen requirement decreased in verum versus sham	3
Usichenko et al. (2005a,b)	THA	61	AA (31)	SA (30)	Opioid requirement	Opioid requirement decreased in verum versus sham	4
Sator-Katzenschlager et al. (2006)	Oocyte aspiration	94	EAA (32) AA (32)	No acupuncture and no electrical stim (30)	Opioid requirement Pain intensity	Pain intensity and opioid requirement was highest in control (non-intervention) group	4
Michalek-Sauberer et al. (2007)	Molar extraction	149	EAA (76) AA (37)	No acupuncture and no electrical stim (36)	Opioid requirement Pain intensity	No differences among groups	4
Usichenko et al. (2007)	AKA	120	AA (61)	SA (59)	Ibuprofen requirement	Ibuprofen requirement decreased in verum versus sham	4

Likar et al. (2007)	LapNE	44	EAA (21)	AA without electrical stim (20)	Opioid requirement Pain intensity	Both parameters reduced in verum group versus sham group	3
Kager et al. (2009)	Tonsillectomy	33	EAA (17)	EAA-Placebo	Pain intensity Analgesic requirement	Pain less in EAA group	4
Yeh et al. (2010)	Spine surgery	94	Acupressure (36)	No acupressure	Pain intensity Analgesic requirement	No difference	3
Holzer et al. (2011)	Gynaecological surgery	40	EAA (20)	Placebo	Pain intensity Analgesic requirement	No difference	4
Tsang et al. (2011)	Hysterectomy	48	TENS (16)	Placebo (16), no intervention (16)	Pain intensity	Less pain only in TENS group	4
Chang et al. (2012)	TKA	62	Acupressure	Sham acupressure	Analgesic requirement Knee motion	Less analgesic requirement and better knee motion in acupressure group	3
He et al. (2013)	TKA	90	Acupressure	Sham acupressure	Pain intensity Analgesic requirement Side effects of analgesia	Less pain, analgesic consumption and side effects of analgesics in acupressure group	4

AA, auricular acupuncture; AKA, ambulatory knee arthroscopy; EAA, electro auricular acupuncture; LapNE, laparoscopic nephrectomy; SA, sham acupuncture; ST, standard therapy; stim, stimulation; THA, total hip arthroplasty; TKA, total knee arthroplasty.



**Figure 10.9** Points taken for acupressure with embedded *Vaccaria* seeds MA-AH3 (knee joint), MA-TF1 (Shenmen), MA-AT1 (thalamus) and MA-AH7 (sympathetic) in the study of [He et al. \(2013\)](#). Four points of the helix were used for control procedure.

**TABLE 10.2** ■ Opioid-sparing effect in treatment of postoperative pain

Intervention	Control condition	Number of patients	Opioid-sparing effect (%)	References
Acetaminophen	P	265	20	<a href="#">Remy et al. (2005)</a>
Ibuprofen	P	406	22	<a href="#">Southworth et al. (2009)</a>
Metamizol	P	162	34	<a href="#">Chaparro et al. (2012)</a>
Auricular acupuncture	S	61	35	<a href="#">Usichenko et al. (2005a,b)</a>
Auricular acupressure	S	90	20	<a href="#">He et al. (2013)</a>

P, placebo; S, sham.

## CHRONIC PAIN

In their systematic review on auriculotherapy for pain management, Asher et al. retrieved five RCTs on the treatment of chronic pain with auricular stimulation ([Asher et al., 2010](#)). Four of these reported the benefits of auriculotherapy in treatment of patients with chronic pain. In particular, the overall change in pain intensity shows significant improvement for acupuncture treatment versus control (SMD 1.84, 95% CI 0.60, 3.07). When poor quality studies were removed, results still favoured auriculotherapy (SMD 2.86, CI 0.70, 5.02). One of the high quality investigations ([Alimi et al., 2003](#)) reported the use of AA in treatment of patients with cancer pain.

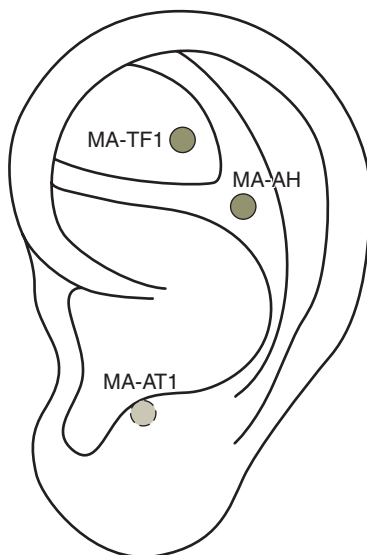
In this study, 90 patients who received standard analgesic medication for cancer pain were randomly divided in three groups; one group received AA at points with reduced skin impedance, and two placebo groups received either AA or auricular seeds fixed at placebo points – identified by normal skin impedance. Pain intensity decreased by 36% at 2 months from baseline in the group receiving acupuncture; there was little change for patients receiving placebo (2%). The difference between groups was statistically significant ( $P < 0.0001$ ) the patients clearly enjoyed the clinically relevant benefits of auriculotherapy.

### Clinical points

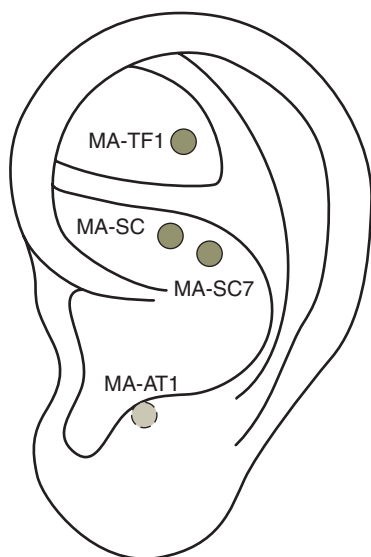
Reasonable evidence supports the use of AA for chronic pain.

Asher et al. (2010) reviewed two investigations where electrical stimulation of AA points was used to treat patients with chronic musculoskeletal pain. It is generally accepted that electrical stimulation of acupuncture points (electroacupuncture, EA) increases the effects of acupuncture. Research groups from Austria reported the use of auricular EA device, the P-Stim™, in treatment of acute perioperative and chronic musculoskeletal pain (Sator-Katzenschlager and Michalek-Sauberer, 2007). In chronic cervical and low-back pain, auricular EA was more effective than conventional AA, with long-term medical and economic benefit. The treatment schedule for patients with low-back pain involves continuous auricular EA with 1 Hz biphasic constant current of 2 mA applied to MA-TF1 (Shenmen), MA-AT1 (thalamus) and MA-AH (lumbar spine) of the dominant side (Fig. 10.10). The effect was compared to the group without electrical stimulation (sham-EA). Treatment was performed once weekly for 6 weeks. Pain relief was better in the EA group during the study and the follow-up period as compared with the group without stimulation. Similarly, psychological well-being, activity and sleep were improved in EA group, the consumption of analgesic rescue medication was less, and more patients returned to full-time employment.

Low-back pain in pregnant women is one of the most common reasons for sick leave during pregnancy Norén et al. (2002), but the analgesic arsenal in this period is restricted for safety



**Figure 10.10** Points MA-TF1 (Shenmen), MA-AT1 (thalamus) and MA-AH (lumbar spine) were used for treatment of chronic low-back pain using electroacupuncture (Sator-Katzenschlager and Michalek-Sauberer, 2007).



**Figure 10.11** Points MA-TF1 (Shenmen), MA-SC (kidney) and MA-SC7 (analgesia) were used in treatment of women with pregnancy-related low-back pain (Wang et al., 2009).

reasons. Wang et al. (2009) advocate AA to relieve the pain and disability in women with pregnancy-related low-back pain. The authors performed 1 week of continuous AA in pregnant women with low-back and posterior pelvic pain and compared the effect of acupuncture with sham procedure and ‘waiting list’. Acupuncture was applied to the points MA-TF1 (Shenmen), MA-SC (kidney) and MA-SC7 (analgesia) using indwelling fixed needles (Fig. 10.11). All 152 patients were monitored for 2 weeks, and the women in the acupuncture group reported a significant reduction of pain and improvement of functional status as compared with those in the sham acupuncture and control groups.

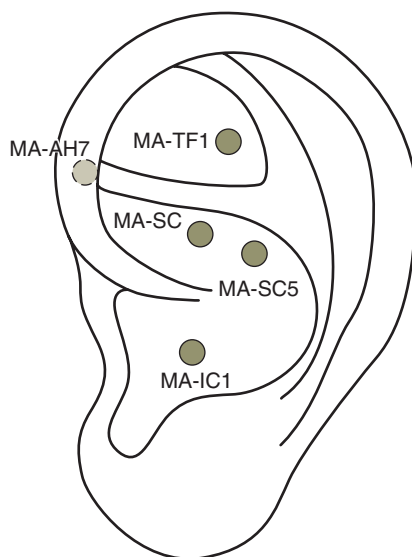
## Drug dependence

### NADA PROTOCOL

Auricular electrostimulation was successfully used by Wen and Cheung in Hong Kong to relieve opioid withdrawal signs in addicted patients (Wen and Cheung, 1973), see Chapter 26 (Drug Dependence and obesity). Later, based on findings of Wen and Cheung, auricular needling without electrostimulation was introduced in the USA for treatment of substance abuse. The standard pattern of 5 AA points – MA-TF1 (Shenmen), MA-SC (kidney), MA-SC5 (liver), MA-IC1 (lung) and MA-AH7 (sympathetic) (Fig 10.12) – received the name of NADA (National Acupuncture Detoxification Association) protocol when it became standardised within the treatment sessions of this organisation (Shwartz et al., 1999). Later the NADA protocol was used worldwide to treat cocaine, heroin and alcohol dependence. The most influential reports on the evidence of AA for cocaine and nicotine dependence are discussed later.

### COCAINE DEPENDENCE

A research group from Yale University evaluated the effects of AA in treatment of 82 patients with cocaine addiction (Avants et al., 2000). The patients, who were maintained on methadone,



**Figure 10.12** Points from NADA (National Acupuncture Detoxification Association) protocol: MA-TF1 (Shenmen), MA-SC (kidney), MA-SC5 (liver), MA-IC1 (lung) and MA-AH7 (sympathetic).

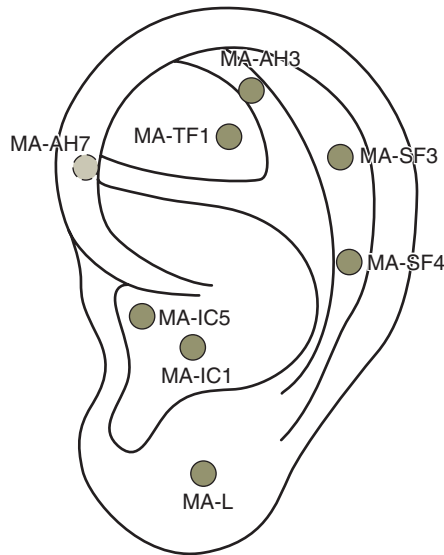
were randomly assigned to one of three conditions: AA according to NADA protocol, a needle-insertion control condition, or a no-needle relaxation control. Treatment sessions were provided five times weekly for 8 weeks. The primary outcome was cocaine use assessed by three-times-weekly urine toxicology screens. The analysis showed that patients assigned to acupuncture were more likely to provide cocaine-negative urine samples relative to both the relaxation control ( $P=0.01$ ) and the needle-insertion control ( $P=0.05$ ). These exciting results could not be confirmed in a large multicentre RCT, performed later by the same research group. Six hundred twenty cocaine-dependent patients were included in the same 3-arms study design, as described earlier (Margolin et al., 2002). Although the analysis of urine samples showed an overall reduction in cocaine use ( $P=0.002$ ), no differences for acupuncture versus both control conditions were seen.

D'Albarto (2004) performed a systematic review of the RCTs on treatment of cocaine abuse with AA. He retrieved six studies (including both RCTs cited earlier) and concluded that the existing trials based on the NADA protocol could not confirm the effectiveness of AA on treatment of cocaine abuse (D'Albarto, 2004). However, acupuncture treatment of drug abuse is still included in the record of WHO as one of the 42 medical problems suitable for acupuncture treatment (WHO Library, 2003).

## SMOKING CESSATION

In a literature review, White and Moody (2006) studied whether AA applied to 'correct' points on the external auricle is better than the stimulation of 'incorrect' points. The authors found 13 studies and concluded that AA appears to be effective for smoking cessation, but the effect may not depend on point location.

A recent RCT by Wu et al. (2007) studied the same question. The authors randomised 131 adults who wanted to stop smoking into two groups. The treatment group received AA in MA-TF1 (Shenmen), MA-AH7 (sympathetic), MA-IC5 (mouth) and MA-IC1 (lung) points for 8 weeks. The control group received sham acupuncture in non-smoking-cessation-related auricular acupuncture points MA-AH3 (knee), MA-SF3 (elbow), MA-SF4 (shoulder) and MA-L



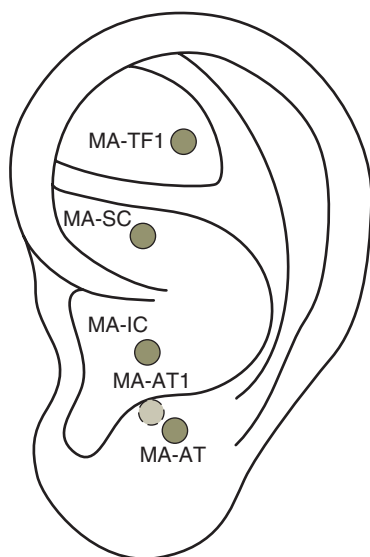
**Figure 10.13** Points MA-TF1 (Shenmen), MA-AH7 (sympathetic), MA-IC5 (mouth) and MA-IC1 (lung) were used to treat smoking cessation by [Wu et al. \(2007\)](#).

(eye) points ([Fig. 10.13](#)). The enrolled subjects were then followed monthly for 6 months after stopping the acupuncture treatment. At the end of treatment, cigarette consumption had significantly decreased in both groups, but only the treatment group showed a significant decrease in the nicotine withdrawal symptom score. The smoking cessation rate showed no significant difference between the treatment group (27.1%) and the control group (20.3%) at the end of treatment. The authors concluded that a combination of AA with behaviour counselling or with nicotine replacement therapy should be used in further smoking cessation trials to enhance the success rate of smoking cessation.

The Cochrane review of acupuncture for smoking cessation, though showing no convincing effect of acupuncture overall, found a short-term effect of continuous auricular stimulation compared with sham stimulation ([White et al., 2014](#)) in a subgroup of 14 RCTs. The risk ratio was RR 1.69 (95% CI 1.32–2.16). Interestingly, the pooled results were positive for the subgroup of seven studies using acupressure but not for the six that used acupuncture with semipermanent needles. The effect persisted only as a non-significant trend at the 6–12 month follow-up.

## Insomnia

In a systematic review, [Chen et al. \(2007\)](#) summarised the results of six RCTs on the efficacy and safety of AA for treatment for insomnia and identified the most commonly used auricular acupuncture points for treating insomnia. The frequency analysis revealed that six commonly used auricular acupuncture points were MA-TF1 (Shenmen) at 100%, MA-IC (heart) at 83%, MA-At (occiput) at 67%, MA-AT1 (subcortex) at 50%, Brain and MA-SC (kidney) – each at 33% ([Fig. 10.14](#)). A meta-analysis showed that improvement rates provided by AA were higher than those of diazepam ( $P < 0.05$ ). Subgroup analysis revealed that AA exerted the maximal effect if it was used for enhancement of sleeping hours up to 6 h ( $P < 0.05$ ).



**Figure 10.14** Points frequently used to treat insomnia: MA-TF1 (Shenmen), MA-IC (heart), MA-AT (occiput), MA-AT1 (subcortex) and MA-SC (kidney).

Another systematic review by [Lee et al. \(2008\)](#), retrieved 10 RCTs on the effectiveness of AA for treating insomnia and confirmed the conclusions of the previous one about the weak evidence for the effectiveness of AA for the symptomatic treatment of insomnia. The authors of both reviews recommended rigorously designed trials to confirm the preliminary results, described in the reviews.

## Other clinical indications

Because AA is an easily performed intervention with very low risk of adverse events, it is promoted in treatment of many conditions where current therapies show inadequate effects. Probably for this reason, research into the effects of AA has often been conducted poorly in recent years. For example, [Zhang et al. \(2010\)](#) retrieved five RCTs in their systematic review of AA treatment of allergic rhinitis. The impact of auriculotherapy could not be evaluated because of the poor quality of included trials. The same conclusions were drawn by [Li et al. \(2010\)](#), in their systematic review of the trials on AA for constipation. The authors retrieved 29 relevant clinical studies, all of which reported that auriculotherapy was effective in managing constipation. However, the unclear descriptions of acupuncture points and subjects' compliance to instructions as well as inconsistent intervention protocols and therapeutic outcome criteria made meaningful comparison among different studies impossible ([Li et al., 2010](#)).

## Adverse events associated with AA

Serious adverse events due to AA are very rare ([White, 2004](#)). The most common complication of AA described in the literature is local infection due to *Staphylococcus aureus* (which exists as a saprophyte on the skin without producing lesions), requiring local and systemic antibiotic therapy. Undiagnosed and inappropriately treated, these cases might merge into a 'worst case scenario' with

persistent perichondritis and subsequent irreversible deformation of the pinna (Gilbert, 1987). However, severe complications like chondritis (with and without permanent deformation of the auricle) described in case reports were the consequences of penetrating trauma of the auricular cartilage with staples (Allison and Kravitz, 1975; Morgan, 2008; Winter and Spiegel, 2010). Needles that penetrate through the cartilage of the auricle may produce the same lesions of the cartilage. Baltimore and Moloy (1976) described a 54-year-old woman who developed perichondritis after the insertion of 4 mm needles into the helix of the pinna. *S. aureus* was isolated from this lesion, which was treated by immediate removal of the needle and intravenous antibiotic. The patient recovered completely and had no scarring.

Reading the case reports, it has not escaped notice that almost all patients experiencing infectious complications of AA were older than 50 years and had concomitant diseases or risk factors, which compromised the microcirculation (e.g. diabetes mellitus, smoking, etc.). Our records from more than 600 patients who received AA with indwelling fixed needles preoperatively for complementary intraoperative analgesia and for treatment of postoperative pain within prospective RCTs revealed none of previously mentioned adverse effects (Usichenko et al., own observations). We used indwelling fixed needles with maximum length of 1.5 mm, retained *in situ* for 24–72 h.

## RECOMMENDATIONS HOW TO AVOID ADVERSE EFFECTS

In addition to the general advice in Chapter 14 (Safety), based on our own experience and a cumulative review of adverse events associated with acupuncture (White, 2004), when providing AA it is expedient to:

- puncture with the patient well supported (e.g. sitting in an armchair) since vasovagal reactions may happen – in which case the patient needs to be laid supine;
- ensure puncture sites are ‘socially’ clean;
- avoid needling (choose acupressure instead) in patients with risk factors: cardiac valve disease, diabetes mellitus, suppressed immunity, significantly low platelet count; and
- advise the patient on the risk of infection and how to identify and manage it safely.

## Concluding comments

Auricular stimulation may be used in the treatment of different types of pain, and the best evidence currently exists for AA in treatment of postoperative pain. Since the options of modern pharmacotherapy are limited in treatment of patients with chronic pain, auricular stimulation can be used additionally or even as a sole therapy. AA is a promising option for treatment of preoperative anxiety and insomnia. Further evidence should be awaited before using AA for other indications in psychiatry, such as substance abuse and mood disorders. AA is an inexpensive intervention, and associated with very low risk of adverse events.

The existing evidence for positive clinical effects of AA in treatment of pain and psychiatric disorders points towards the potential mechanisms of AA at the level of brainstem. These mechanisms involve the cranial nerves and their nuclei as well as cerebral endogenous neurotransmitter systems.

The most exciting question for future investigations is individual responsiveness to auricular stimulation. This can be addressed in both experimental and clinical research, but laboratory studies seem to offer more opportunities to classify an individual as ‘AA responder’ or ‘non-responder’ and to search for the causes of this phenomenon.

The clinical effect of AA can be enhanced by a continuous mode of stimulation (e.g. indwelling fixed needles or electrical current). More accurate and reliable estimates of the effect will require large, well-designed trials and researchers should consider introducing new objective methods of measurement of pain, such as imaging.

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# Electroacupuncture

D.F. Mayor

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## Introduction

Electroacupuncture (EA), defined as the passage of a pulsed electric current through the body tissues via one (or more) pairs of acupuncture needles for therapeutic purposes (White, 1998), has been used widely since the late 1970s. Its history, however, stretches back further, to the very beginnings of acupuncture practice in the West in the early nineteenth century.

Although European publications on different aspects of acupuncture practice and Chinese medical theory date back to the last years of the seventeenth century, the first Westerner known to have actually needled patients was Dr Louis Berlioz (father of the composer) in 1810 (Barnes, 2005). He did not follow the complex and subtle Oriental approach but simply inserted common sewing needles directly into areas of pain for 4–5 min (Berlioz, 1816). Six years later, he proposed that the direct current from Alessandro Volta's electric battery might enhance the effect of the needles by stimulating and replenishing the nerves (Berlioz, 1816). Perhaps because his work had already been criticised as 'somewhat reckless' by the Société Médicale in Paris (Quen, 1975), he never seems to have done this himself, but his suggestion was taken up in 1823 by a fellow Frenchman, the rather more flamboyant Jean-Baptiste Sarlandière, Chevalier d'Honneur of the Kingdom of Prussia, inventor of the mechanical leech, and friend of the experimental physiologist François Magendie (van Heiningen, 2009).

Sarlandière's 'electropuncture' employed gold and silver needles inserted through a guide tube and retained for 5–10 min. He found that direct current of 'reasonable intensity' could

‘modify pain, motion or capillary circulation’ (initially he also used static discharges through the needles) (Sarlandière, 1973). Conditions treated included rheumatism and gout, asthma and migraine, various forms of paralysis, dysmenorrhoea and various ‘nervous afflictions’. He preferred to stimulate muscle rather than the nerves directly and cautioned against using electricity where major inflammation is present.

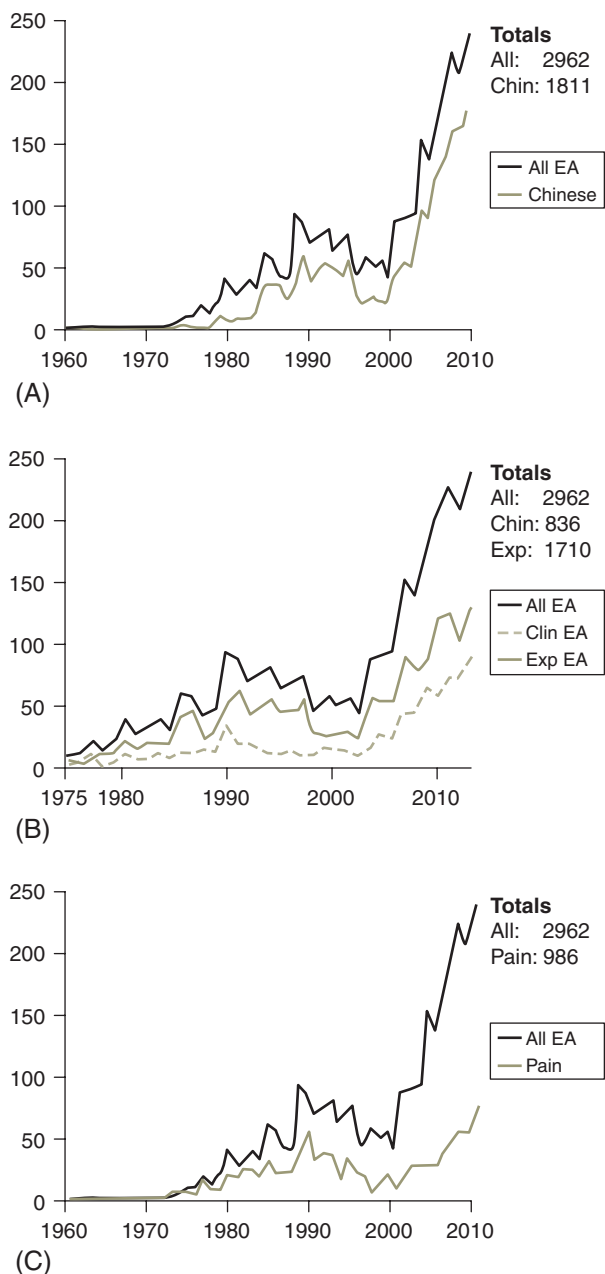
Along with acupuncture, EA became fashionable in the 1820s and 1830s in Europe and America but was soon overtaken by the developing field of non-invasive electrotherapy, as well as by other medical fads such as mesmerism. Although still occasionally used, it was not until the 1950s that it resurfaced in any major way. In Japan and the West, this was at first primarily in the form of electrical diagnosis (Ryodoraku (Hyodo, 1975), EA according to Voll (Rondé, 1998)), which will not be considered further here. In China, the story was rather different.

As part of Chairman Mao’s efforts to control the intelligentsia, in the mid-1950s modern doctors were made to study traditional medicine (Croizier, 1976). By 1958, the emphasis was more on integration of the two systems (Lucas, 1982), as evident in Joseph Needham’s observations of the use of EA for some 70 different conditions at a clinic in Xian (Lu and Needham, 1980). At the same time, China was not wealthy, and general anaesthetics for example were not widely used. Thus it is not surprising that in the same year first acupuncture, and then EA, known for their effects on pain (and postoperative pain in particular), were first applied in an attempt to reduce the pain experienced during surgery. To begin with, machines were developed to rotate the needles mechanically and so obtain a comparable sensation to *de qi* (Chapter 3), but then these were (mostly) superseded by EA devices that provided electrical stimulus directly to the needles without the need for mechanical rotation. This was really the birth of what became known as ‘acupuncture anaesthesia’ or ‘acupuncture analgesia’ (AA) or, more accurately, ‘acupuncture hypalgesia’, although a few animal experiments on AA had already been carried out in France (Maric, 1979). In the 1960s, state manufacture began of the G-6805 stimulator (Yang and Yang, 2010), prototype for many later EA devices, yet still available today in various updated models.

Showcasing AA, particularly when using EA (EAA), was one way of demonstrating China’s national progress and scientific advances to the outside world, and much research was conducted into the mechanisms involved, particularly from 1956 at the Shanghai Institute of Physiology (and later the Shanghai Brain Research Institute) under Chang Hsiangtong (Zhang Xiangtong) (Zhang, 1986), and from 1965 by the Research Group for Acupuncture Analgesia in Beijing, spearheaded by Han Jisheng (Han, 2009). Because EA offers a more readily controllable and measurable stimulation than traditional manual acupuncture (MA), it has been commonly used in such experimental research. A PubMed search shows, for example, that 48% of the 3344 animal acupuncture studies published between 1975 and 2011 involve EA in some way (annually,  $45.8 \pm 15.8\%$ ) (Mayor, 2013).

From the late-1970s there have been many publications on EA by Chinese authors, and since around 1985 they have dominated the field in most years, at least in terms of sheer numbers of studies produced (Fig. 11.1A). There have also always been more experimental EA studies (on mechanism or basic science) than clinical ones (see Fig. 11.1B). However, the very first EA study (1956) located in the China National Knowledge Infrastructure (CNKI) database of China Academic Journals was one on the treatment of headache, and in most early publications there was little emphasis on clinical applications other than for pain. Today this has changed, with increasing evidence that EA can, like MA, be used for a far wider spectrum of conditions (see Fig. 11.1C) (Mayor, 2013).

This chapter provides an overview of EA, in which the basic parameters of electrical stimulation are described, differences between EA and MA sketched, and the endorphin model summarised. A review of the clinical applications of EA is provided, with suggestions on the appropriate acupuncture points and parameters to use. Precautions, contraindications and practicalities are covered. The chapter ends with a short section on the advantages of EA over MA, some thoughts on effective therapeutic ‘dose’, and a look at how EA may develop in the future.



**Figure 11.1** EA publications listed in PubMed, 1960–2011. **(A)** Chinese preeminence in the field of EA research (includes studies with Chinese lead authors). **(B)** Most published EA studies are experimental rather than clinical. **(C)** Early EA research was mostly on pain, but subsequently non-pain dominated. **(B and C,** reproduced from Mayor, D.F., 2013. *An exploratory review of the electroacupuncture literature: clinical applications and endorphin mechanisms*. *Acupunct. Med.* 31 (4), 409–415, with permission.)

# Electrical stimulation parameters

Before using EA in the clinic, it is necessary – as with any form of electrotherapy – to know a little about electricity and the physiological effects of electrical stimulation.

The electric current (flow of charge) used in EA has various characteristics: polarity, frequency, amplitude/intensity, mode, pulse duration and waveform. These are very different from those used by the early pioneers such as Sarlandière, being based on technology that was not available in their time. These are dealt with in turn.

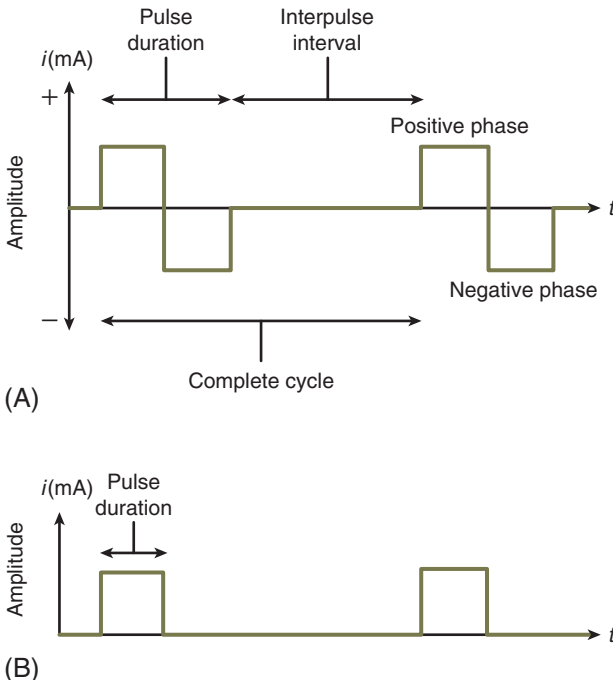
## POLARITY

Current should ideally be biphasic (as in alternating current) rather than monophasic (as in direct current). In other words, current should flow one way and then the other way between the needles, rather than always in the same direction (Fig. 11.2).

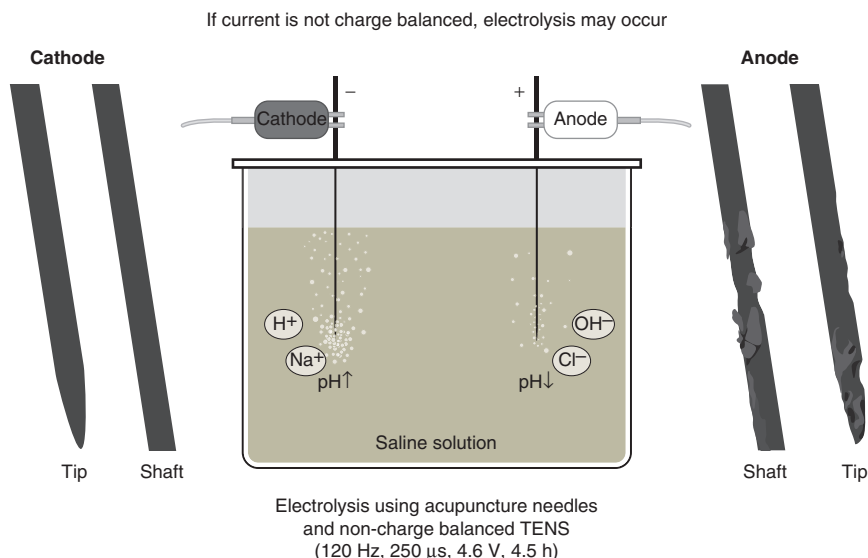
Furthermore, the waveform should be ‘charge-balanced’, meaning that the total quantity of charge transferred in each direction should be equal, with minimal residual charge remaining at each needle electrode between pulses. If direct or monophasic currents are used, or stimulation is not charge-balanced, there is a risk of electrolytic breakdown of the needle, particularly at its tip and at the skin (Hwang et al., 2010), with potentially adverse effects (Fig. 11.3).

## Clinical points

The waveform produced by an electroacupuncture device should ideally be biphasic and charge-balanced.



**Figure 11.2** (A) Biphasic square wave current. (B) Monophasic square wave current. This figure also shows pulse duration. (Adapted from Mayor, D.F. (Ed.), 2007a. *Electroacupuncture: A Practical Manual and Resource*. Churchill Livingstone, Edinburgh (CD-ROM version), with permission.)



**Figure 11.3** Electrolysis of needles when testing a device for charge-balance. Note corrosion of the more positive needle at its tip (where current density is greatest) and also where the shaft passes through the surface of the saline solution (and the capacity for ion diffusion is reduced). (Photographs courtesy of Riccardo Cuminetti.)

In this respect, EA differs from transcutaneous electrical nerve stimulation (TENS) (Chapter 15), where charge-balance is not so critical given that the electrode-tissue contact area is much greater (typically, 1600–2500 mm<sup>2</sup> as against about 20 mm<sup>2</sup> for a 0.25 mm diameter needle inserted 25 mm), and so the charge density is considerably less.

## FREQUENCY

*Frequency* (pulse repetition rate or number of pulses delivered per second, whether these are biphasic or monophasic as in Fig. 11.2) is measured in Hertz (Hz) or ‘cycles per second’. In EA, a ‘low frequency’ (LF) is approximately 2–4 Hz and ‘high frequency’ (HF) is 50–200 Hz.

Traditional MA involves needle manipulation in the form of rotation or lifting and thrusting, something which can only be done at LF. EA, originally designed to mimic such movements, at first followed suit – in contrast to TENS in the West, which conventionally involves HF stimulation.

## Clinical points

The most important frequency in EA treatment is likely to be 2–4 Hz.

## AMPLITUDE/INTENSITY

Depending on the type of equipment used, the *amplitude* of the output (see Fig. 11.2) may be a measure of current or voltage. In EA, maximum amplitude may be of the order of 12 mA (milliampères), or 9 V (volts), but these figures will vary considerably depending on equipment design and will take account of safety issues for the particular device in question. For comfort, a number of EA stimulators today are ‘constant current’ devices, which means that the output current does not fluctuate, whatever the impedance (resistance to biphasic current flow) at the needle/body interface. The output amplitude control then gives an indication of how much current is flowing.

The strength or *intensity* of sensation experienced by the patient depends on amplitude more than on frequency. Almost all patients will describe 6 mA or above as ‘strong’ (Cummings, 2011a). Sometimes it is more meaningful to describe the level of stimulation in terms of intensity than amplitude – as ‘sensory’ (noticeable, above sensory threshold, around 0.3–1.0 mA), ‘motor’ (resulting in muscle twitching, at 0.5–0.8 mA if the needle is close to a motor nerve, or 1.0–1.5 mA elsewhere in muscle tissue (Cummings, 2011a)) or ‘noxious’ (frankly painful, from around 10 mA). However, these thresholds are individual. They also depend on pulse duration and the position of the needle tip.

### Clinical points

The typical intensity for therapeutic EA treatment is 1–3 mA.

## PULSE DURATION

The duration of each individual pulse (see Fig. 11.2) is an important variable, although preset in most standard EA devices. When using LF, it is usually in the region of 200  $\mu$ s, whereas for HF, it is rarely greater than 100  $\mu$ s. Thinner afferent nerve fibres, such as the thinly myelinated A- $\delta$  or unmyelinated C (temperature and pain) fibres, require longer pulse durations to trigger an action potential and thicker myelinated fibres, such as A- $\alpha$  (motor) or A- $\beta$  (mechanoreceptor, sensory) fibres require shorter pulse durations. Standard strength-duration curves indicate that the threshold for nerve fibre activation depends on both pulse duration and current amplitude (Cramp and Scott, 2008), in other words on charge per pulse (charge = duration  $\times$  amplitude). Increasing this will recruit more fibres.

## MODE

Stimulation may be continuous (CW) (as in Fig. 11.2A), intermittent (burst), ‘dense-disperse’ (DD, alternating higher and lower frequencies, usually above and below 30 Hz, respectively (Wang et al., 2010)), or otherwise modulated (Fig. 11.4).

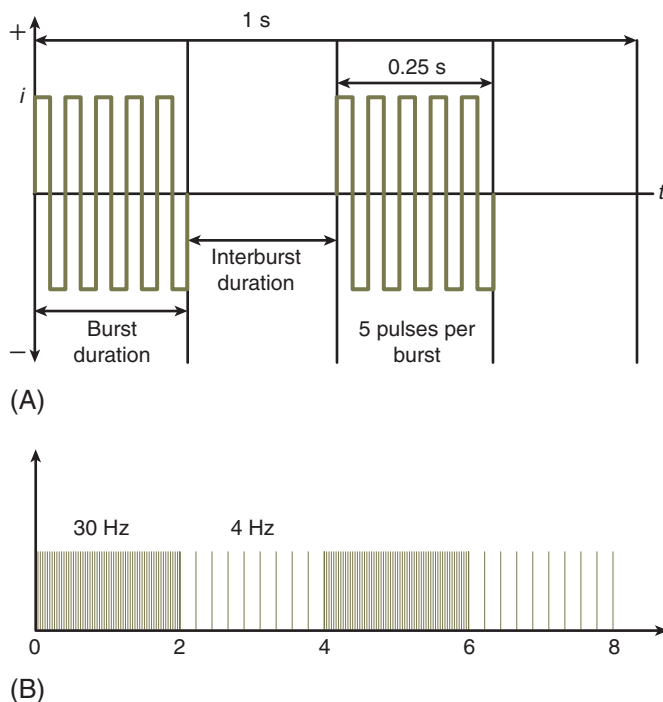
With intermittent ‘trains’ or bursts of pulses at a given frequency, e.g. 2 Hz (see Fig. 11.4A), the pulse charge required to trigger a neuronal action potential is less than for isolated pulses at the same frequency. Thus pulse trains can be an efficient (and more comfortable) form of stimulation (Eriksson and Sjölund, 1976).

## WAVEFORM

We usually think of ‘waves’ as sine waves. In EA, however, the rise time of each pulse has to be brief to elicit an action potential, so square (or rectangular) pulses are now mostly used, as illustrated here, although some EA devices produce spike or other waveforms (a comprehensive review is provided by Mayor (2007a) and a briefer one from the Chinese perspective by Hong and Liu (2006)).

## STIMULATION RANGES

It is helpful to consider two main types of stimulation: LF/high intensity/longer pulse duration (subjectively strong, though still tolerable) and HF/low intensity/shorter pulse duration (subjectively gentle and comfortable). Because of the way these were developed and researched – the former predominantly as EA in China and the latter predominantly as TENS in the West – they can be thought of as ‘acupuncture-like stimulation’ and ‘TENS-like stimulation’, whether they are applied through needles or surface electrodes. LF bursts are sometimes described simply as LF in



**Figure 11.4** (A) 2Hz intermittent (or ‘burst’) current, with an internal frequency of 20Hz. (B) Dense-disperse mode (4/30Hz DD), repeating every 4s. (Adapted from Mayor, D.F. (Ed.), 2007a. *Electroacupuncture: A Practical Manual and Resource*. Churchill Livingstone, Edinburgh (CD-ROM version), with permission.)

the literature. Other combinations are of course possible, but these are the most commonly used, together with their alternation in DD mode (although too often this is merely an alternation of frequencies, without consideration of amplitude or pulse duration).

## TREATMENT DURATION

Optimal duration is usually taken to be 20–30 min, with little advantage from longer periods of treatment (Lundeberg, 1984), though in experimental studies useful results have been reported with 15 (Toda et al., 1980) or even 10 min of stimulation, as in a number of earlier reports by Han and his collaborators (Han, 1987).

### Clinical points

The optimum duration for therapeutic EA treatment is 20–30 min.

## Similarities and differences between manual and electrical stimulation

Needling itself (MA) is usually intended to elicit the *de qi* response of aching, soreness, pressure, heaviness and/or distension (fullness) (Hui et al., 2007) and is considered to activate predominantly A-δ fibres, although A-α, A-β and C fibres may also be involved in its effects (Carlsson, 2002), depending in part on the technique used. A-α activation may result in muscle twitch, A-β

in numbness and tingling (Hui et al., 2007) and C fibre activation in sensations of frank pain, warmth or coolness. One way of activating the A- $\delta$  (and possibly C) fibres is through strong repetitive muscular contraction (see Chapter 3, Neurophysiology), which has led some researchers to investigate similarities in the neurophysiology of EA and physical exercise (Andersson and Lundeberg, 1995). On the other hand, the conceptual basis of traditional acupuncture does not depend on the activation of physiological responses (Li et al., 2012): some methods of MA elicit very little (Baldry, 2005) or even no (Huang et al., 2008a) sensation on the part of the patient, and muscle contraction, although perhaps desirable, is not a necessary concomitant of EA (Nappi et al., 1982; Tougas et al., 1992).

Locally, tissue injury (Cabioglu and Cetin, 2008) may contribute to the after-effects of needling, while changes also result from release of vasoactive and pro-inflammatory neuropeptides from A- $\delta$  and C fibres (Carlsson, 2002). The primary afferents themselves synapse with other ascending neurons in the dorsal horn (directly or via linking interneurons), leading to further activation of a number of complex spinal and supraspinal mechanisms (Bowsher, 1998; White, 1999). In turn, within the brain many different regions may be activated or deactivated by MA (Hui et al., 2010). Some of these are in the brainstem and also contribute to autonomic regulation (Lundeberg, 1999). The antinociceptive effects of MA are explained by the involvement of several descending inhibitory systems (Bowsher, 1998; White, 1999), the more systemic effects of MA by its involvement in autonomic regulation (Lundeberg, 1999).

Prior to the application of EA, needles are inserted and *de qi* obtained (although not all expert practitioners insist on this). Just as for MA, it is important to avoid or minimise sharp pain on needling, although dull pain may be acceptable (Hui et al., 2010). Thereafter there are several differences between the two methods:

- EA provides rhythmic stimulation that is more prolonged.
- The intensity of stimulation will usually be greater than that of MA (but sometimes MA is greater for brief periods, depending on the style of MA practised).
- The frequency of stimulation may be very different from that of MA.
- EA will often (but not necessarily) result in repeated localised muscle contractions.

## Neurophysiology: the endorphin model

Serendipitously, acupuncture and the endorphins both became hot topics of research in the mid-1970s, and it is often stated that acupuncture ‘releases endorphins’. However, most of the evidence for the acupuncture-endorphin connection has been derived from studies on EA, not MA (Hammerschlag and Lao, 2001), and to make sense of this statement, it needs to be examined in more detail.

To this end, reports of studies of acupuncture and endogenous opioid mechanism were located by extensive searches. When these were analysed, they showed that 49% of studies of MA, compared with only 17% of studies on EA/TEAS (transcutaneous electrical acupoint stimulation), showed no effect on opioid release (Mayor, 2013). This implies that the effects of EA are more likely to be due to opioid peptide release than the effects of MA. Taking the analysis further, Table 11.1 shows the corresponding figures for different frequencies of stimulation.

The figures in these tables reflect many complex factors, such as gender differences (Bossut et al., 1991), variations in responsiveness (Raevskaia, 1992; Sekido et al., 2003), situational context (e.g. stress (He, 1987)) or cumulative effects (Bossut and Mayer, 1991; Liang et al., 2010; Liu et al., 2010; Stener-Victorin and Lindholm, 2004). There is also the difficult issue of how far it is possible to extrapolate results based predominantly on experimental animal studies to humans, whether clinical patients or healthy subjects (although Han for one does not consider this a problem (Han, 1987; Han, 1998)). One should also consider the evident preponderance of EA studies in research on opioid mechanisms, likely publication bias (e.g. non-publication of negative outcomes or ‘political

**TABLE 11.1 ■ Correlation of frequency of stimulation with opioid release: numbers of EA/TEAS studies in PubMed (Searched 2011) showing endogenous opioid release (negative studies in parentheses), by organ or tissue**

Studies	Brain	Spinal cord	Blood	Other tissue	Not specified	Negative (%)	Total EOM studies for modality
LF (1–7 Hz)	81 (2)	27 (3)	20 (8)	6 (0)	56 (13)	14	190
8–10 Hz	12 (0)	6 (0)	2 (2)	0 (1)	2 (3)	27	22
14–17 Hz	6 (1)	2 (0)	5 (0)	0 (0)	6 (0)	5	19
20–30 Hz	5 (0)	1 (0)	1 (0)	3 (0)	7 (0)	0	17
43–50 Hz	2 (1)	0 (0)	2 (1)	0 (0)	5 (1)	33	9
HF (≥80 Hz)	22 (3)	11 (3)	2 (1)	1 (0)	16 (11)	35	52
DD (2/15 Hz <sup>a</sup> )	15 (0)	8 (0)	2 ↓ (1)	1 (0)	5 (0)	3	31
DD (10/20 Hz <sup>b</sup> )	6 (0)	0 (0)	0 (2)	1 (0)	0 (0)	29	7
DD (LF/HF)	6 (0)	3 (0)	3 [2 ↓] (2)	2 (0)	4 (1)	17	18
DD (undefined)	6 (0)	1 (0)	0 (0)	0 (0)	1 (0)	0	8
Other	3 (0)	1 (0)	3 (1)	0 (0)	2 (0)	11	9
Parameters unknown	8 (2)	2 (1)	2 ↓ (0)	0 (0)	10 (0)	14	22

↓ indicates a decrease in blood  $\beta$ -endorphin in response to stimulation.

A fuller version of this table has been published elsewhere (Mayor, 2013).

EOM endogenous opioid mechanisms

<sup>a</sup>Including 2/12 and 6/18 Hz.

<sup>b</sup>Including 6/25, 5/30 and 10/30 Hz.

correctness' (Chapman et al., 1983; Mayor, 1997)) and errors or misinterpretations when dealing with the multiple neural circuits involved (Bossut et al., 1991). Even so, certain trends are apparent:

EA studies are more likely to be positive for opioid involvement than MA studies since:

1. Increased levels of endorphins in the central nervous system (CNS) in response to EA – whether HF or LF – are more likely than increases in the blood levels, although this may not be the case for MA.
2. LF – particularly acupuncture-like – stimulation involves opioid release relatively consistently, whereas HF (or TENS-like) stimulation, even at around 45–50 Hz, is less likely to. However, this difference is less clear-cut at intermediate frequencies (e.g. 8–10 Hz).

There are several factors that limit the strength of these conclusions, which are fully discussed elsewhere (Mayor, 2013). There is good evidence that both MA and EA may cause release of opioid peptides (Mayor, 2007a), so apparent differences may be due to the greater 'dose' of EA, methodological differences between studies in terms of timing and duration of stimulation, variations in responses to opioid receptor antagonists, and the development of tolerance from prolonged or over-frequent stimulation, explainable as resulting from the release of the endogenous peptide cholecystokinin (CCK-8) (Han, 1995). It does seem clear that acupuncture effects in the EA studies were more likely due to central opioid release than stimulation of the pituitary.

In summary, acupuncture-like stimulation is usually explained – mostly on the basis of animal studies – as activating various endorphinergic 'long-loop' supraspinal pathways (some of which may also be involved in the opioid mechanisms of MA), with  $\mu$  or  $\delta$  ORs involved in the spinal cord (Chen and Han, 1992b); and HF or TENS-like stimulation is explained as promoting dynorphin release at the spinal level (DD at 2/15 Hz may involve both mechanisms (Chen and Han, 1992a)). In other words, the effects of acupuncture-like stimulation will spread both spatially and temporally, having an extrasegmental or systemic effect that may take some time to build up

but then lasts beyond the period of stimulation, whereas those of TENS-like stimulation are more limited, pretty much to within the segment stimulated and only while stimulation continues (Kim et al., 2004; Mayor, 2007a, CD; Silva et al., 2011). However, in practice LF EA is most commonly applied segmentally (see Table 11.4).

In addition to the differences in opioid involvement between MA and the various commonly used modes of EA (LF, HF, DD, etc.), a number of fMRI studies have demonstrated that they have different patterns of brain area activation and inactivation (Kong et al., 2002; Zhang et al., 2003; Napadow et al., 2005), just as for different frequencies of TEAS (Jin et al., 2001). Thus all forms of stimulation, whether MA, EA or TEAS, will have supraspinal effects, even though these effects may differ. If one modality is not effective, it may be worth trying another.

DIFFERENCES IN EFFECTS OF MA AND EA

Results from the accessible studies comparing MA and EA located using PubMed are shown in Table 11.2.

Disregarding questions of bias or study quality, this is at least indicative that the effects of EA are often greater than those of MA (Box 11.1).

Clinical indications for EA

In order to identify the main clinical indications for which EA is used, a review was conducted of the study design of all located published RCTs using EA up to 2011. The full report is available in Mayor (2013), but the salient information is summarised in Table 11.3. In addition,

TABLE 11.2 ■ Results of studies comparing EA and MA

	EA > MA	MA > EA	EA = MA	EA ≠ MA
<i>Experimental</i>				
Animal	13	5	13	2
Human	12	3	1	3
<i>Clinical</i>				
Human	29 <sup>a</sup>	2 <sup>b</sup>	6	1

>, significantly superior; =, no difference; ≠, effects not quantitatively comparable but different.

<sup>a</sup>In one of these studies, the addition of EA to MA improved outcome.

<sup>b</sup>In one of these studies, the addition of MA to EA improved outcome.

BOX 11.1 ■ Comparing EA with TEAS

If EA activates primarily A-δ fibres (but also A-α, A-β and sometimes C fibres), TEAS activates primarily A-β fibres (but also A-α and, if strong, A-δ fibres in animals, though maybe not in humans).

However, very few RCTs that compare these modalities could be located. In two Swedish papers on stroke by the same group (Johansson et al., 2001; Rorsman and Johansson, 2006), effects were comparable, as they were in a Chinese mixed pain study (Fang et al., 1999). In a Chinese stroke study, however, EA had larger effects (Huang et al., 2008b), while in two related studies comparing a new Chinese type of TEAS device with EA, the device (predictably) appeared to give better results (Cui et al., 2009; Yang et al., 2009). Thus clinical results are inconclusive, although TEAS may well have advantages in terms of cost-effectiveness, for example, if used by patients themselves to enhance practitioner-delivered EA.

**TABLE 11.3 ■ Summary of main features of RCTs of EA for different conditions, 1974 to early 2012**

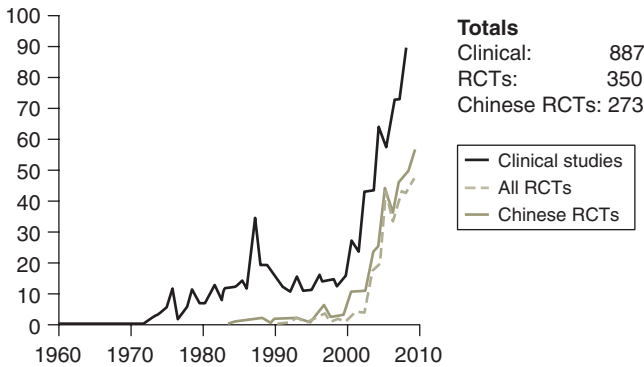
Condition	N RCTs	Points used	Parameters used
Addiction	13	9a 6m 5s [3 sa] 1t	4LF 5HF 4DD
Weight loss	14	5a 7m 9s 11t	7LF 2HF 4DD 1×20Hz
Cardiovascular	8	1a 4m 1s 6t	2LF 2HF 2DD 1×20Hz
ENT	10	3a 6m 8s [3 sa] 4t	4LF 1HF 3DD 2×10Hz
Peripheral motor disorders	15	7m 15s [1 sa] 8t	8LF 1HF 4DD 1i
Gastrointestinal	32	2a 21m 20s 25t	9LF 5HF 10DD 4×10Hz 1r
Musculoskeletal	90	3a 20m 79s [3 sa] 21t	37LF 5HF 16DD 5×10Hz 4×15Hz 1×20Hz 3×(30–50Hz) 3r
Neurology	47	1a 24m 42s [23 sa] 11t	16LF 13HF 6DD 1×10Hz 3×15Hz 1×20Hz 1r 2i
Peripheral neuropathic pain	3	2m 3s	2LF 1HF 1DD
Chronic/neuropathic pain (other)	2	1m 1s	2DD
Mixed pain	1	1m 1s	1LF 1HF
Head/facial pain	6	1a 1m 2s 3t	1LF 1HF 3DD
Obstetrics and gynaecology	32	1a 24m 25s 20t	10LF 3HF 14DD 1×10Hz 1×15Hz 1×20Hz 1×50Hz 1i
Genito-urinary	16	8m 16s [3 sa] 9t	9LF 1HF 3DD 2×10Hz 1×20Hz 1i
Psychiatry	26	2a 4m 24s [25 sa] 7t	15LF 4HF 4DD 1r
Respiratory	3	1m 2s 2t	1HF 2DD
Intraoperative analgesia &c	32	3a 27m 22s [1 sa] 9t	12LF 9HF 14DD 1×10Hz 1r
Postoperative analgesia &c	32	5a 22m 19s [1 sa] 12t	11LF 7HF 5DD 1×10Hz 1×20Hz 4r
Cancer care	1	1a 1m 1s 1t	1LF
Endocrinology and chronic fatigue	3	3m 2s [1 sa] 3t	1LF 1HF 1×20Hz 1×50Hz
Dermatology	3	1a 2s 2t	2DD 1r
Animal studies	2	1m 2s 1t	2DD
Totals	391	38a 191m 301s [63 sa] 156t	150LF 63HF 101DD 17×10Hz, etc.

*Notes: Some studies covered several conditions and others were reported more than once; such duplicates were not removed. Types of points used are divided into 'a' (auricular), 'm' (major, see text), 's' (segmental), 'sa' (scalp acupuncture, including traditional head points) and 't', traditional/meridian (mostly non-segmental). Some of these categories overlap, but virtually no points are excluded using these groupings. Parameters used: LF, low frequency; HF, high frequency; DD, dense-disperse (alternating frequencies); i, intermittent; r, range. Around 60% of DD studies used alternating LF and HF, but others used combinations such as LF/15Hz or LF/20Hz.*

Figure 11.5 demonstrates the rapid increase in annual publication rates of RCTs categorised as involving EA, as well as the continuing dominance of Chinese studies in the literature.

The review gives an indication of the scope and commonly accepted features of EA practice (interestingly, those conditions considered as good candidates for EA by Sarlandière nearly 200 years ago are still well represented). However, it cannot cover what is done in the individual and often more complex cases that escape the narrow inclusion criteria of most RCTs. This should be borne in mind when using EA: clinical reasoning and an awareness of what is being communicated in the patient-practitioner feedback loop should take precedence over formulaic approaches. For these reasons, like other forms of acupuncture EA should only be used after adequate training, rather than merely learned from a book.

Results of our review are summarised in Table 11.3, which shows numbers of RCTs for each set of conditions. Points and parameters used are discussed in the next section.



**Figure 11.5** EA clinical studies and RCTs listed in PubMed, 1960–2011. The Chinese RCTs include those by Western research groups with Chinese lead authors.

## EA: ACUPUNCTURE POINTS AND PARAMETERS USED IN PRACTICE

Table 11.3 shows that segmental points are the most commonly used (in 77.0% of studies), often in association with one or more from a shortlist of well-known ‘major’ points (48.8%). As discussed earlier, and from Chapter 7, it is clear that EA for a localisable or segmentally defined condition, applied at local or distal points within the segment, may have different effects from EA applied heterotopically, that is in unrelated segments, whether at distal or contralateral points.

Local intrasegmental points that tend to be used include those reactive to pressure (*ashi*), meridian or other traditional points, trigger points (TrPs), and even motor points (MPs).

Extrasegmental points might be distal meridian points or also TrPs or MPs. However, in practice a limited number of familiar ‘major’ points familiar from traditional practice tend to be used, particularly PC6, TE5, LR3, LI4, ST36 and SP6 (of which LI4 and ST36 are also MPs).

For non-segmental (e.g. systemic) problems, the major points are most used. Those familiar with TCM syndrome differentiation may add other traditional or empirical points, although these are more often needed traditionally rather than with EA.

For both segmentally and non-segmentally defined conditions, ‘microsystem’ EA is a possibility, most commonly using ear or scalp points (Chapter 10). The latter are frequently used in neurological or psychiatric conditions.

Of course, clinical reasoning may be applied using either biomedical or TCM models, as in the treatment of osteoarthritis of the knee, for example, where some groups justify point selection on the basis of neurophysiology and anatomy (Näslund et al., 2002), while others select the identical points on the basis of TCM theory and experience (Berman et al., 1999).

As for the electrical parameters of treatment, from Table 11.3 it is clear that LF EA was much more commonly used (38.4%) than HF (16.1%) – except perhaps for addiction – and that DD stimulation was also common (25.8%), particularly (but not exclusively) in gastrointestinal, musculoskeletal and intra/postoperative studies where pain was the main concern. Intriguingly, 10 Hz EA also occurred, but was not common (2.6%). Most (59.4%) of the DD studies used a standard 2/100 Hz (HL), but quite a number (20.8%) preferred to alternate low and ‘low-mid’ range (8–25 Hz) frequencies.

Table 11.4 shows the most used point types and stimulation frequencies in the studies we reviewed. Many studies included various point categories, and some compared EA at different frequencies, so were counted more than once. The different modes of EA (acupuncture-like/LF, TENS-like/HF and DD) were introduced earlier. In addition, low-midrange frequencies (broadly around 8–20 or 25 Hz, or more specifically at 10–15 Hz) were used more than might be expected.

Intrasegmental EA (whether LF or HF) in healthy subjects was found in one seminal study to have more effect on dental pain threshold than extrasegmental EA at LI4 (a ‘major’ point)

**TABLE 11.4 ■ EA acupuncture points and stimulation frequencies used in RCTs, 1974–2012, showing numbers of each point category for the main parameter types**

Parameters	N points/ parameter	Segmental/nerve <sup>a</sup>	Major <sup>b</sup>	Traditional	Auric	Scalp
LF (0.5–7 Hz)	248	109 (C 62; CL 2)	35 (C 10; CL 2)	60 (C 32; CL 3)	20 (C 3; CL 1)	24 (C 20; CL 1)
Low-midrange (8–25 Hz)	68	30 (C 17; CL 1)	19 (C 9)	12 (C 7; CL 1)	1 (CL 1)	6 (C 6)
HF (≥30 Hz)	130	50 (C 41)	37 (C 25; CL 1)	22 (C 19; CL 1)	9 (C 4)	12 (C 12)
DD (LF/HF)	125	40 (C 32; CL 2)	37 (C 31; CL 1)	40 (C 35; CL 2)	5 (C 1)	3 (C 2; CL 1)
DD (Mid/HF)	9	5 (C 2)	3 (C 2)	1 (C 0)	0	0
DD (LF/Mid)	65	25 (C 20)	18 (C 16)	17 (C 14)	0	5 (C 5)
Range	29	13 (C 5)	7 (C 2; CL 1)	6 (C 3; CL 1)	3 (C 1)	0
Totals	674 <sup>c</sup>	272	156	158	38	50

Numbers are approximate because of imprecise descriptions in some Chinese studies; 35 studies (not all conducted in China) were excluded because of insufficient information on stimulation parameters.

C, Chinese authors; CL, lead author Chinese but study not conducted in China.

<sup>a</sup>Two Chinese studies referred to specific nerve pathways rather than segmental distribution.

<sup>b</sup>The 'segmental' category often included 'major' points not listed separately here (especially if 'local' as well as 'segmental'), but the 'scalp' and 'segmental' frequently overlapped, as did 'major' and 'traditional'.

<sup>c</sup>Because of overlaps, this total is not meaningful.

(Lundeberg et al., 1989). The data here suggest that segmental acupuncture points are in fact the most commonly used, followed by the major points. However, DD with a HF component is relatively less used segmentally than at the major points, and for segmental stimulation LF EA is clearly used considerably more often than HF EA, despite theoretical support for the latter as outlined previously (and an as yet unsupported suggestion that the ‘wind-up’ pain-inhibiting effect induced by repetitive C fibre stimulation (Gebhart and Jones, 1988) may also occur with non-noxious HF EA (Lin et al., 2002)). Given that acupuncture-like stimulation has more widespread effects than TENS-like stimulation, and that EA was first exploited in a major way as a replacement for the LF needle manipulation of MA, this is not really surprising. As for microsystem EA, it appears that scalp/head EA is more commonly described in Chinese studies and auricular EA in non-Chinese studies. Again, this might be expected, given that auricular acupuncture originated in France (Gori and Firenzuoli, 2007) and scalp acupuncture in China (Liu et al., 2012).

Box 11.2 shows some examples of ‘most used’ parameters and points for some common conditions. It is not possible to suggest protocols here for more than a handful of conditions. For other conditions, readers are advised to consult other sources (Mayor, 2007a,c) and to browse journals such as *Acupuncture in Medicine*.

#### BOX 11.2 ■ Examples of ‘most used’ parameters and points for some common conditions

##### **Migraine (Mayor, 2007d)**

Local/segmental points: GB8, GB20, ST8, *Yintang* (M-HN3), *Taiyang* (M-HN9)

Distal (major) points: LR2, LR3, LI4

Parameters: LF CW to tolerance, 20 min

##### **Low back pain with sciatica (Mayor, 2008)**

Local (segmental) points: BL23, BL25, GV3, GV4, *Huatuojiaji*

Distal (segmental) points: along the affected meridian (BL, GB or more rarely ST)

Parameters: LF CW or DD, to tolerance, 20–30 min

##### **Peripheral facial paralysis (Mayor, 2007b)**

Local (segmental) points: GB14, ST4, ST6, ST7; also TE17, LI20, ST2, *Taiyang*

Distal (major) point: LI4

Parameters: initially LF, low intensity, 15–20 min; later stronger (motor level), 20–30 min

##### **Knee osteoarthritis (Royal London Hospital for Integrated Medicine group clinic protocol, modified from Cummings protocol)**

Local (segmental) points: ST33–ST36 and SP10–SP9

Parameters: 2/15 Hz DD, to tolerance, 30 min

##### **Chronic shoulder pain – adhesive capsulitis or rotator cuff tendinopathy (Cummings protocol)**

Local (segmental) points: LI15–LI16 and TE14–SI11 (or a trigger point in infraspinatus near SI11)

Parameters: 2/15 Hz DD, to tolerance, 30 min

##### **Lateral epicondylalgia (Cummings protocol)**

Local (segmental) points: two pairs of points on the affected side at LI11–LI10 and a pair of needles onto the epicondyle (needle tips aimed into the most tender area)

Trigger points can be used instead of LI10, with a common connection to LI11.

Parameters: 2/15 Hz DD, to tolerance, 30 min

##### **Pathophysiological conditions of the pelvic viscera eg irritable bladder, dysmenorrhoea, sub-ovulatory polycystic ovary syndrome (Cummings protocol modified from Stener-Victorin)**

Segmental points: four pairs of points at ST27–ST28 and SP6–LR3 bilaterally

Parameters: 2/15 Hz DD, to tolerance, 30 min

## EA – precautions and contraindications

These comments, based on a paper by [Cummings \(2011a\)](#), apply specifically to EA and assume the reader is familiar with the normal precautions and contraindications for MA, as discussed in [Chapter 14](#).

### NEEDLE DEPTH AND ANGULATION

Practitioners should take into account how needles might move in response to repeated muscular contraction. There is a risk of organ damage if they penetrate too deeply or of needle damage if they penetrate multiple muscle layers that do not contract uniformly.

#### Clinical points

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Consider how needles may move with involuntary muscle contraction caused by EA.

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### NEEDLE LOCATION

In principle, needles should not be positioned directly over the heart or so that current flows through the chest ([Wang et al., 2010](#)). Although the risk of ventricular fibrillation only becomes significant at around 50 mA ([Ward, 2006](#)) and most patients will not tolerate more than about 6 mA for long, higher currents could be applied inadvertently if a stimulator develops a fault. Additional risks arise if a needle is inserted close to implanted leads. In the special case of patients with leads placed directly into the heart (e.g. pacemakers, intracardiac defibrillators or some types of central line/catheter), currents as low as 0.1 mA applied to these leads may be fatal ([Ward, 2006](#)). Nonetheless, EA and TEAS studies with bilateral stimulation of upper limb points (e.g. PC6 or LI4) have been conducted in healthy experimental subjects ([Lundeberg et al., 1989](#)), in patients ([Feng et al., 2007](#); [Ni et al., 2009](#); [Shen et al., 2009](#)) and in animals ([Wang et al., 2005a](#)) without reported adverse effects, and sometimes with obvious benefits ([Cheung and Jones, 2007](#)), even following open-heart surgery ([Ng et al., 2011](#)).

#### Clinical points

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Do not apply current across the chest or near to implanted leads.

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It is commonly stated that EA should not be applied from one side of the head to the other or one ear to the other, for fear of current flowing through the brain ([Wang et al., 2010](#)). However, the electrical resistance of scalp tissues is much lower than that of the skull, so current will flow preferentially through the scalp, not the brain, and so there is very little risk of an adverse effect on the brain. This is borne out by the fact that EA between points such as GV20 and *Yintang* is commonly used. However, some Chinese authors still discourage the use of EA at any scalp points ([Lü, 2009](#)).

Needle pairs from the same output may be positioned on either side of the spine, apart from in the chest region. This is also the case for TEAS, as in one RCT on chronic obstructive pulmonary disease, COPD ([Lau and Jones, 2008](#)).

Stimulation should not be applied to the anterior triangle of the neck, either over the carotid sinus (e.g. at point SI17) because of effects on the baroreceptor reflex or to the nerves that supply the laryngeal muscles (e.g. at point ST9) because of the risk of airway restriction, particularly at HF ([Sanders et al., 1987](#)). Stimulation of the vagus nerve via points such as SI17, ST9 or ST10 may induce bradycardia.

Bearing in mind that the electrical potential between two inserted needles resulting from EA may affect quite an extended region, it was previously recommended that needles are not inserted either side of a metal prosthesis (Myklebust and Robinson, 1989). However, most authorities do not consider this a problem (Bazin et al., 2008), and certainly a pair of needles from the same output can safely be inserted proximal to the prosthesis, another output pair distally. Scrupulous cleanliness of technique is needed in such cases, to avoid infection at the prosthesis site.

## ELECTRICAL PARAMETERS

If a stimulator is used that is not charge-balanced, there is a risk of electrolysis of the needles (Cummings, 2011b; Yi et al., 2011). TENS machines are not necessarily charge-balanced so should never be used for EA without prior testing. Some EA devices produce charge-balanced currents at low amplitudes and frequencies but not at higher ones so should be used accordingly (e.g. the KWD-808II Multi-purpose Health Device, manufactured in China (Mayor, 2007a; Miao, 2011)).

Another reason for not using TENS machines is that they are designed to pass current through surface electrodes and the skin, not through the needle/tissue interface, which has a much lower electrical impedance. They produce far higher currents than required for EA, usually exceeding the safe level of 50 mA. Some dual-purpose devices do, though, incorporate a range switch to ensure that the output remains well below this level when used for EA. If this is the case, routine procedural checks for EA should involve ensuring that the machine is set to the correct range.

Most EA equipment is battery-powered, but some come with an adaptor to enable treatment while the device is plugged into the mains supply. This should be used only if designed explicitly for medical application (with proper isolation and patient leakage current  $\leq 10 \mu\text{A}$ , or  $50 \mu\text{A}$  under single fault condition) (British Standards Institute, 2006). Otherwise any fault could result in a potentially dangerous mains electric shock.

As Sarlandière noted, strong stimulation may aggravate an already inflamed or hyperaesthetic area (as in some neuralgias, fibromyalgia or chronic regional pain syndrome, CRPS). For this reason, individual patient sensitivity should always be taken into account.

HF, high amplitude EA that induces tetanic muscle contraction will not be tolerated for long by most patients.

## INTERACTION WITH OTHER DEVICES

Another serious concern is the use of EA when a patient is fitted with a device such as an implantable cardioverter defibrillator (ICD) or pacemaker. These may be sensitive to the levels of current used in EA (Fujiwara et al., 1980; Lau et al., 2005; Graf and Pruvot, 2007). As discussed earlier (See Needle location) needles should be inserted so that current does not flow anywhere near the device or any implanted leads that make contact with cardiac tissue – so in the leg, for example, rather than above the waist (Rasmussen et al., 1988; Sliwa and Marinko, 1996; Thompson and Cummings, 2008) although lumbar stimulation may be safe (Vasilakos and Fyntanidou, 2011)). In one interesting study, EA was used for inflammatory wrist pain at Heart-associated (TCM concept, non-segmental) local points without problems in a patient with a total artificial heart (Gopalan et al., 2011). However, if in doubt it is always wise to take advice from the patient's cardiologist.

### Clinical points

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If a patient has an ICD or pacemaker, it is wise to consult their cardiologist before using EA.

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Potentially, interactions may occur with implanted devices such as insulin pumps and hearing aids, or with nearby high powered medical microwave or shortwave equipment, but to our knowledge these have not been reported and will be avoided if EA is not used when these other devices are active.

## PARTICULAR CONDITIONS

Restrictions in the use of EA close to a tumour in patients with cancer to the head or neck, close to the foetus in pregnancy (Bazin et al., 2008) and in patients who are liable to seizures are discussed here.

As high intensity/LF EA has the potential to increase vasodilatation locally (Chen and Yu, 1991; Lin et al., 2003), albeit not above physiological levels, there is a small risk that it may lead to the spread of metastases.

Strong somatosensory stimulation has been reported to trigger seizures under some circumstances (Rosted, 2001), although EA has been used in the treatment of epilepsy (Cheuk and Wong, 2008; Mayor, 2007c). EA could also conceivably induce arrhythmia or a hypertensive episode in someone with poor cardiovascular health. However, to our knowledge this has not been reported in practice and, again, EA has been used to treat both these conditions (Kang and Xia, 2009; Mayor, 2007c; Wan et al., 2009). Clearly, patients should be carefully monitored if they are liable to seizures, have a heart condition or have experienced a haemorrhagic stroke.

Clinical studies have been conducted using TEAS for pregnancy-related nausea (Helmreich et al., 2006) and using EA in pregnant animals (Guerreiro da Silva et al., 2011), and although the consequences of using EA during the first trimester are unknown, there is no plausible physiological mechanism of harm from sensible use of the technique. However, EA tends to be reserved for use later during pregnancy, particularly to induce labour (Lim et al., 2009).

Theoretically, there may be cross-tolerance between acupuncture-like stimulation and opioid medication, with the implication that those receiving acupuncture-like stimulation may not respond so well to these drugs, and those who have taken them for a while may not respond well to acupuncture-like stimulation (Léonard et al., 2011). In contrast, postoperatively amitriptyline may be a useful adjunct to EA, whether LF or HF (Fais et al., 2012a,b). Other drug-EA interactions are also possible (Appendix 3 in Mayor, 2007a).

In summary, many of the safety implications of applying electrical stimulation at acupuncture points are theoretical. Practitioners should therefore not be discouraged from using EA but should use their clinical judgement in taking account of the issues detailed here. Reports in the literature of serious adverse events that relate to the electrical stimulus as opposed to the trauma of needling have been systematically reviewed by Zheng et al. (2012), who concluded that most may be attributed to 'improper operation'. They included death from spinal cord injuries (needles deeply inserted in the neck and suboccipital region) and from cardiac rupture after sternal needling. They also reported atrioventricular block caused by needling at *Anmian* (between TE17 and GB20); excessive stimulation leading to fracture of the femur head; dislocation of the wrist joint and several cases of nerve injury, including one of neuroparalytic keratitis. One patient had an electrical 'burn', and two were reported with exacerbation of gastric ulcer in association with EA, though not necessarily attributable.

## EA – SOME PRACTICALITIES

EA should be used, bearing the earlier precautions in mind, when indicated, for example when a condition has not responded to a few sessions of MA.

Not all patients will willingly accept EA. Some may have received electric shocks in the past or may be suspicious of a non-traditional approach to acupuncture. Some may be too sensitive (in which case they may anyway respond well to MA, although the modern devices that control current in steps of 0.1 mA can be used on anyone without risk of overstimulation); and some may feel the sensation is too weird so strong stimulation cannot be given (particularly if muscle contraction results). To instil confidence, the method, its purpose and the sensations to be expected should all be described before obtaining consent and commencing treatment.

Many different EA stimulators are available, each with particular advantages and disadvantages. Most will be adequate provided they are CE-marked (or FDA- or TGA-approved) as being designed for this purpose (*not* just for TENS), with a charge-balanced output that can be accurately adjusted (both in terms of frequency and amplitude), and providing at least CW and DD (or equivalent) modes. Whatever equipment is used should be regularly maintained and serviced and the supplier notified in case of equipment failure or adverse effect. Batteries should be replaced regularly, as treatment may become ineffectual if they are low.

Needles should be electrically conductive and not too thin (0.25–0.30 mm is a suitable diameter for standard use, although thinner needles may be used on the face or in other areas where bleeding is to be avoided). On insertion, in the Chinese studies *de qi* is usually elicited at each point, although this is considered probably unnecessary by many Western medical acupuncturists. However, if needle sensation is sharp in nature on insertion, the needle should be repositioned for comfort before clipping the stimulator lead to a clean part of the needle (2–3 mm above the skin or at the base of the handle if it is metal). Leads or needle handles can be taped to the skin to help prevent needles penetrating more deeply or falling out on muscle contraction. Once parameters have been selected and frequency/frequencies set, amplitude can be turned up slowly until the patient feels the stimulation sensation – initially as a tingling or buzzing, perhaps followed by other feelings conventionally described as ‘fullness’, ‘numbness’ or ‘soreness’ (Wang et al., 2011). It is helpful to advise patients that sensation should remain ‘strong but comfortable’. When the sensation has become familiar, amplitude can be further increased. It may not be possible to turn this up very high in the first session, but at subsequent visits patients may tolerate stronger stimulation, particularly if they are given control of the output (after clear instruction). Care should always be taken to titrate stimulation according to patient response and not to increase amplitude too rapidly, as output controls may not be linear (particularly with cheaper machines) and even a slight increase may take the sensation from comfortable to painful. You may wish to ask the patient to describe what is felt; they should feel free to tell you if it becomes too uncomfortable (this may well vary between sessions and even depend on the acupuncture points used).

Stimulation should be continued for 20–30 min (so ensure the patient is comfortable before starting). In most situations, more will not be necessary. Patients should not be left without some method for contacting the practitioner, and should not be left unattended at all if unduly nervous or suffering from one of the conditions mentioned previously. If they have to be left, they should be instructed in how to turn off the EA device. All device settings should be recorded in the patient notes.

## Concluding comments

EA – like technology in general – is no panacea and may initially appear to add an unnecessary level of complexity to medical acupuncture. However, when used appropriately, it can certainly improve outcomes, often potentiating the effects of traditional methods or dry needling.

Its advantages over MA include:

1. more effective in some situations
2. less time consuming than repeated manipulation of needles
3. less demanding of the practitioner, in both training and practice, compared to traditional MA techniques
4. good results may occur with EA when there has been no obvious benefit from MA
5. allows stronger, more continuous stimulation with less tissue damage
6. more readily controlled, standardised and objectively measurable.

There are few disadvantages in using EA: it may take slightly longer to set up a treatment than with MA, and there is a greater risk of over-treatment if used without due consideration.

Routine use may also inhibit the subtle interactions of the therapeutic relationship. In the end, however, whatever the practical advantages and disadvantages, and whatever the evidence, deciding whether or not to use EA is often more a matter of personal preference than anything else.

Despite considerable advances in understanding, there is still controversy over which parameters of EA are the most important in establishing an effective therapeutic ‘dose’, whether frequency (Han, 1998) or amplitude (Barlas et al., 2006; Mayor, 1997), for example. Perhaps this is simply a question of total monophasic charge per treatment, which is a function of both these variables, as well as of pulse and treatment duration, although possibly independent of the number of points stimulated (Wang et al., 2005b; Zhou et al., 2005). For contrasting findings on this issue, see for example Toda et al. (1980) and Cassu et al. (2008), as well as the TENS literature (Claydon et al., 2008). There is also little detailed knowledge of the body’s own bioelectrical responses to different parameters of stimulation (even in the EEG and ECG, for example). Furthermore, the basic concepts and technology of EA have changed little over the last half-century, and given the costs of developing new methods of treatment and their delivery, this situation is not likely to change very fast. In China, where EA is much more accepted and researched (with nearly 15 500 publications listed by CNKI up to 2012, as against just over 3000 for *all* countries in PubMed), the situation is very different. Despite China’s strong tradition of cultural conformity, there is less bureaucratic restraint on technical innovation, particularly where it is obviously progressive and modernising. Examples are the SXDZ-100 TEAS device, whose output is claimed to encode data collected from dorsal horn wide dynamic range (WDR) fibres in response to traditional needle manipulation (Gao et al., 2012), ‘uni-acupoint’ stimulation designed to obviate the need for two needle insertions (Niu et al., 2009), and audio frequency (music) ‘pulse width modulation’ TEAS to minimise tolerance (Hong and Liu, 2006; Xiong et al., 2011). Whether these innovations will really revolutionise the practice of EA or are merely another example of minor trends in the history of acupuncture, only time will tell.

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# Self-acupuncture

M. Forrester

## CHAPTER OUTLINE

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## Introduction

Self-acupuncture has been used for hundreds of years. Ever since Willem Ten Rhijne described the first case of self-acupuncture in 1683 (Carrubba and Bowers, 1974), there has been the phenomenon of self-treatment in this area of therapeutics. Reports of self-acupuncture largely disappeared from the literature but survived in the indigenous culture of China and Japan. In this chapter we will explore the history, contemporary context, safety, training and possible future directions of self-acupuncture.

## Definition

Before we start our exploration of self-acupuncture we should define what we mean by 'self-acupuncture'. Self-acupuncture has been written about many times (Bishop, 2008; Campbell and Hopwood, 2004; Cummings, 2008; Fagan and Staten, 2003; Filshie, 2006; Filshie et al., 2005; Filshie and Hester, 2006; Filshie and Rubens, 2011; Foell, 2011; Google, 2012; Orpen et al., 2004; Sandberg, 2006; Teig et al., 2006) but only recently defined (Dyer et al., 2013).

Since no definition of self-acupuncture could be found in the literature or on an internet search, a small group of colleagues agreed on the following definition for self-/home-acupuncture (SHA):

*Self-acupuncture or home-acupuncture is acupuncture performed by a patient or patient's acupuncture partner, following assessment and appropriate training by their attending regulated health care professional.*

Dyer et al. (2013).

## History

While Willem Ten Rhijne (1647–1700) was serving as a physician in Japan with the Dutch East India Company (1674–76), he witnessed self-acupuncture and later described it (Ten Rhijne, 1683). Translated from Latin, it reads: ‘My guide for the journey to court, a garrison soldier of the Emperor of Japan, had emerged from a holocaust and, being exceedingly hot, he drank enough cold water to quench his thirst. A terrible pain, but one which did not radiate to his flanks, seized his stomach. ... In my presence he performed the acupuncture in the following manner ... Lying on his back, he drove the needle into the left side of his abdomen above the pylorus at four different locations. ... While he tapped the needle with a hammer (since his skin was rather tough), he held his breath. When the needle had been driven in about the width of a finger, he rotated its twisting-handle. He pressed the location puncture by the needle with his fingers. No blood, however, appeared after the extraction of the needle; only a very slight puncture mark remained. Relieved of the pain and cured by this procedure, he regained his health’ (Carrubba and Bowers, 1974).

Self-acupuncture appears again more than 130 years later when Dr Louis Berlioz (1776–1848) treats a young woman in 1810:

*A young person aged 24, who was very good-looking and charming, and of course slim and blonde, was suffering from a 2-year nervous fever brought on by a severe fright. ... She had tried all kinds of treatment previously. After the first needling she improved dramatically. She inserted the needle in her abdominal wall, with excellent though temporary results. Further treatments were required subsequently but 6 months later she was entirely cured (translation, Anthony Campbell).*

Tailleux (1986).

In modern times, two leading practitioners have pioneered SHA. Campbell has been teaching SHA since 1977 when he worked at the Royal London Homoeopathic Hospital (Campbell and Hopwood, 2004). He developed and later published an instruction sheet for use with needles without introducers (Campbell, 2001). Filshie has been teaching SHA for 30 years in the field of cancer care and was involved in the seminal randomised, controlled trial of acupuncture self-needling as maintenance therapy for cancer-related fatigue (CRF) after therapist-delivered acupuncture (Molassiotis et al., 2012, 2013). Filshie and Hester also developed and published an instruction sheet based extensively on that of Campbell, specifically for cancer patients self treating pain or hot flushes (Filshie and Hester, 2006). Other contemporary medical acupuncturists have used and promoted SHA in areas such as chronic musculoskeletal pain.

The reported uses of SHA are listed in Table 12.1.

## Author's experience

In 2002, the author became interested in SHA after discussing with a memorable patient (BB) the possibility of continuing his electroacupuncture (EA) at home, given by his wife, a retired nurse. BB had had extensive neck surgery for cervical radiculopathy in the form of an anterior cervical fusion at C7/T1 for C8 nerve root compression in 2000. Unfortunately, he was left with significant residual pain. This was controlled for up to 7–15 days with EA given to paraspinal points from C3 to C6. He gained ‘almost complete pain relief’ from the EA treatment. Logically what BB wanted was EA every 7–15 days. This was not possible within the resources of a typical hospital health service acupuncture clinic. So, could SHA be used as a way to manage demand (Teig et al., 2006)?

A poster was prepared by the author and BB for a scientific meeting (British Medical Acupuncture Society (BMAS) (Forrester, 2005)) to raise questions and stimulate debate on the topics which should be considered by anyone contemplating SHA (Table 12.2).

TABLE 12.1 ■ Uses of SHA reported in the literature

System	Condition	References
Constitutional symptoms	Cancer-related fatigue	Molassiotis et al. (2013)
	Chemotherapy associated nausea	Adler and Hansen (2012)
	Chronic pain	Teig et al. (2006)
	Cancer pain	Filshie and Hester (2006)
	Nausea and vomiting, postop or chemotherapy	Filshie and Hester (2006)
	Vasomotor symptoms in cancer patients	Filshie et al. (2005) and Filshie and Hester (2006)
	Insomnia	Filshie and Hester (2006)
	Pain	Orpen et al. (2004)
	Vasomotor symptoms caused by tamoxifen	Towlerton et al. (1999)
	Xerostomia	Cheville and Basford (2006)
Ear, nose and throat	Hayfever	Fagan and Staten (2003)
	Meniere's Disease	Fagan and Staten (2003)
	Benign postural vertigo	Fagan and Staten (2003)
Respiratory	Cancer-related dyspnoea	Filshie and Hester (2006)
	COPD-related dyspnoea	Filshie and Hester (2006)
Gastrointestinal	Sphincter of Oddi Dysfunction	Walter and Curtis (2013)
	Radiation rectitis	Filshie and Hester (2006)
	Crohn's disease	Fagan and Staten (2003)
	Ulcerative colitis	Campbell and Hopwood (2004)
Genitourinary	Dysmenorrhoea	Fagan and Staten (2003)
	Detrusor instability	Fagan and Staten (2003)
Musculoskeletal	Postsurgical facial pain	Dyer et al. (2013)
	Osteoarthritis hand and knee	Fagan and Staten (2003)
	Cervical spondylosis	Fagan and Staten (2003)
	Writer's cramp	Fagan and Staten (2003)
	Patellofemoral osteoarthritis	Fagan and Staten (2003)
	Lateral epicondylitis	Fagan and Staten (2003)
	Osteoarthritis thumb MCP joint	Fagan and Staten (2003)
	Achilles tendonitis	Fagan and Staten (2003)
	Rotator cuff strain	Fagan and Staten (2003)
	Subacromial bursitis	Fagan and Staten (2003)
	Postsurgical neck pain	Forrester (2005)
	Back pain	Ewart (1972)
	Ulcers	Filshie and Hester (2006)
Integumentary		
Neurological	Multiple sclerosis	Foell (2011)
	Migraine	Fagan and Staten (2003)
	Postherpetic neuralgia	Fagan and Staten (2003)
Psychiatric	Deliberate self-harm	Davies et al. (2011)

To judge from their responses, the majority of the delegates at that meeting seemed too apprehensive to embrace the concept of SHA. However, this work with BB helped myself and the Pain Clinic, who at the time were using acupuncture for chronic pain management, to write a Clinical Guideline (Priddle and Forrester, 2007), as is necessary before introducing any new technique into the hospital.

TABLE 12.2 ■ Questions to ask about SHA

Patient selection	Is this condition suitable for self-acupuncture treatment? Are some patients more suitable than others to be taught self-treatment? Should patients be taught EA?
Training	What is the appropriate level of training and supervision for safe self-acupuncture? Which acupuncture points and which types of acupuncture are safe for us to teach? Is it safe for us to teach limited acupuncture treatments to patients, or relatives or carers of patients? If the patient is not able to self-treat, is there someone else who could do it? How often should they self-treat?
Service delivery and follow-up	How often should they be followed-up? How often should they or their relatives' practice be monitored and reviewed?
Supplementary questions	Does self-acupuncture empower the recipient to take control of their illness? Does self-acupuncture disenfranchise the therapist? Should introducing 'self-acupuncture' to a health service be seen as a significant service development to be encouraged? Are the published guidelines on SHA comprehensive?

Attitudes of the acupuncture profession towards SHA have become significantly more positive since that date.

## The literature

The literature where SHA is mentioned or formally studied is limited. After Willem Ten Rhijne's report of 1683 ([Ten Rhijne, 1683](#)), no further references can be found until the description by Louis Moss of needling his own back was published in *The Healing Needles* ([Ewart, 1972](#)). Moss was a contemporary of Felix Mann, a pioneer of medical acupuncture.

In the 1980s, [Umeh \(1988\)](#) wrote about semi-permanent needles in the ear and their acceptability in Nigeria. The patients stimulated their semi-permanent ear needles but it is not clear from the paper whether they inserted them also.

Ten years later, Campbell described self-acupuncture in a chapter in *Medical Acupuncture* ([Filshie and White, 1998, p. 29](#)), mentioning its use in patients who respond for 'relatively short periods ... but ... get excellent relief'. Campbell highlighted the importance of patient selection and needling site selection. LR3 and the lower abdomen (though not safe in very thin people) were mentioned as sites that are easy for patients to use, as was the possibility of training a relative to perform the acupuncture. [Towlerton et al. \(1999\)](#) working in Filshie's department reported on a new technique of teaching twelve women with tamoxifen-induced vasomotor symptoms to treat themselves with semi-permanent (Acumedic) needles at SP6, after the initial course of standard acupuncture. The women were taught to change their semi-permanent needles every 10–13 days. Treatment lasted for 4–36 months (mean 13). All but two women tolerated their needles well in the long term, and eight of the twelve had complete or significant reduction in symptoms.

[Campbell \(2001\)](#) expanded on his previous work in the book *Acupuncture in Practice*, where he devotes a chapter to 'Self-treatment with acupuncture'. The same year [Filshie \(2001\)](#) described

do-it-yourself needle kits being commonly used in Cancer Care out-patient for maintenance of symptom control for hot flushes associated with anti-oestrogen treatment. Instruction leaflets, skin cleansing and safe sharps disposal were reviewed.

Fagan and Staten (2003) published an extensive audit of self-acupuncture in primary care. They suggested LI11, LI4, TE3, LR3, SP10, GB31 and BL60 as potentially useful points for SHA. An advice sheet for patients, published as an appendix (p. 31) includes general advice about self-needling, sharps disposal, health care telephone contact information and general do's and don'ts concerning SHA.

Subsequently, Orpen et al. (2004) explored SHA in the secondary care Pain Clinic setting, with an audit addressing the question whether SHA is a safe way to meet increased demand. An established SHA service had been withdrawn because of 'concerns around safety and risks', expansion of the conventional acupuncture service, and lack of experience of SHA from other centres. But with increasing demand for acupuncture, the authors again considered SHA as one possible way of meeting patient demand, but questions about safe practice, patient selection, training, supervision, supply of materials, providing information and potential medico-legal issues still had to be addressed. This article stimulated a debate between two acupuncture authorities with opposing views on SHA (Campbell and Hopwood, 2004). Campbell could see no objection to teaching patients to insert small needles into anatomically safe areas. On the other hand, Hopwood argued that the risks were too high, there were good alternatives to SHA and the patient-therapist relationship was essential.

Filshie et al. (2005) reported a larger audit of 194 patients using self-acupuncture for hot flushes in cancer patients, for up to 6 years. A treatment algorithm was developed that included acupuncture sessions and semi-permanent studs. The authors concluded: 'This treatment has a low incidence of side effects and may currently be the safest form of non-drug treatment' (Filshie et al., 2005, p. 178).

Cheville and Basford (2006), in a small study in xerostomia ( $n=57$ ), showed how spouses (33), parents (6), siblings (5), friends (2) or even children (11) could, easily and successfully, be taught SHA. Also that year, Teig et al. (2006) looked at SHA for chronic musculoskeletal pain in an audit in a secondary care pain clinic. This audit suggested that SHA was effective and improved quality of life. Safety probably depended on patient selection and good training. SHA was seen as a potential tool to reduce clinic waiting lists and appointment times for patients.

Filshie and Hester (2006) published the first guidelines for providing acupuncture treatment for cancer patients. These included guidance and patient instructions on treating pain and hot flushes with SHA, based broadly on suggestions by Campbell (Campbell and Hopwood, 2004). The main points taught were SP6, LR3 and ST36, with additional sites on the body possibly included if 'the patient is deemed sufficiently responsible to carry it out and the point locations are unlikely to do any serious harm'. The same year, Filshie suggested looking further into the use of self-needling (SHA) in relation to the management of bladder disorders with acupuncture, based on her clinical experience (Edwards, 2006). A further formal clinical guideline was published by the present author in 2007 (Priddle and Forrester, 2007).

In 2008, the debate over SHA between two professional bodies was revisited: the BMAS representing mainly medically trained professionals who also practice acupuncture and the British Acupuncture Council (BAcC) mainly representing acupuncturists without additional Western medical training. Cummings (2008) stated there was no formal BMAS policy governing SHA and explained the rationale for the use of SHA, namely for particular indications, i.e. symptom control (Filshie et al., 2005), if it appeared to be in the best interests of the individual patient, and could be taught and delivered with appropriate safety considerations (Campbell and Hopwood, 2004). On behalf of the BAcC, Bishop (2008) expressed a dilemma: traditional training seemed to suggest that it would be unthinkable to advise patients to needle themselves. Yet there were some conditions where the practice had gained some acceptance by the BAcC, namely those in which the circumstances were 'exceptional and well-controlled' (Bishop, 2008, p. 52). Bishop stated that it would be unreasonably harsh to deny a patient pain relief from SHA.

After a hiatus of 3 years, [Filshie and Rubens \(2011\)](#) revisited SHA with reference to palliative care. It was agreed that safety was paramount and that it was important to continue to provide 'top-ups' indefinitely as patients' benefits from each treatment continued to decay. These problems were overcome in various ways including teaching SHA to patients with hot flushes, customised to fit in with their lifestyle. [Foell \(2011\)](#) suggested SHA with added EA as a way of 'helping the ones you cannot help' when treating symptoms in a patient with a chronic neurological condition, multiple sclerosis. SHA has also been studied as a therapeutic regimen for helping patients who deliberately self-harm and appears to have had considerable success ([Davies et al., 2011](#)).

[Adler and Hansen \(2012\)](#) presented a poster showing that patients could safely be taught to use SHA at PC6 during cycles of their chemotherapy regimen. Some evidence suggests that the anti-emetic effects of PC6 stimulation may last about eight hours. Most patients do not have access to a trained acupuncturist at such intervals. SHA seemed to reduce the severity of nausea and reduce the use of anti-nausea medication. Following the theme of oncology, [Molassiotis et al. \(2012, 2013\)](#) studied SHA for cancer-related fatigue (CRF) in patients following chemotherapy for breast cancer in the first large randomised controlled trial in this area. They found SHA to be an acceptable, feasible and safe maintenance treatment for patients with CRF, showing a non-significant trend in reduction of fatigue compared with no acupuncture.

## Safety

Safety is of paramount importance in medical practice, including SHA ([Filshie and Rubens, 2011](#); [Fagan and Staten, 2003](#); [Campbell and Hopwood, 2004](#)). Hopwood ([Campbell and Hopwood, 2004](#)) cites risks of hepatitis transmission, experimentation by patients, one case of exhibitionist SHA resulting in injury and one resulting in death ([Schiff, 1965](#)), as risk factors for SHA that discourage its use.

It is arguable that the risk of home needle-stick injury causing transmission of blood-borne infection to a SHA acupuncturist is extremely small ([Butsashvili et al., 2011](#); [Jason, 2013](#); [Kim and Lee, 2013](#)) and in fact has not been reported ([White, 2004b](#)). People have experimented with needles (known as 'polyembolokoilamania') over the years ([Keogh et al., 1988](#); [Unruh et al., 2012](#)) and have done so with sewing needles ([Schiff, 1965](#)) and acupuncture needles ([Roy, 1974](#)). Even in Japan where self-acupuncture is prohibited by law, five cases (20% of the total) of cervical cord and medulla oblongata injuries were attributed to self-acupuncture ([Miyamoto et al., 2010](#)). There is no evidence to support the idea that teaching SHA encourages patients to experiment with their needles. There are no primary case reports of serious adverse events related to SHA under the direction of a regulated healthcare professional: all the cases of injury and death have been associated with *unsupervised* SHA, and thus it is unhelpful to use these cases as an argument for the potential risk of SHA. Campbell ([Campbell and Hopwood, 2004](#)) did describe a broken needle in LR3 that had to be removed under general anaesthetic. This accident was related to social circumstances rather than the SHA technique. The patient was needling LR3 when someone jumped onto the couch and threw her into the air.

Even a professional acupuncturist has been reported injuring himself: 'In only one case of self-treatment, which caused spinal cord injury, the patient was a licensed acupuncturist' ([Yamashita et al., 2001](#)). [Schiff \(1965\)](#) reported the death from self-needling of a person said to have been an acupuncturist; interestingly she was using a sewing needle to treat herself and not an acupuncture needle. With reference to self-needling over the chest, [Cummings \(2008\)](#) wrote: 'Under no circumstances can I imagine such a technique being recommended for self-treatment'.

Clinical experience strongly suggests that, when carefully trained to perform a limited and easily repeatable therapeutic task, patients and/or their caregivers can be just as skilled in needling as some acupuncturists.

Actions that may reduce the general risks of SHA are listed in [Table 12.3](#).

TABLE 12.3 ■ The basis of SHA good practice

Item	References
<i>Patient selection</i>	
Ensure that the patient, relative or companion is sufficiently competent and reliable	Campbell and Hopwood (2004)
Ensure patient is suitable for self/caregiver needling and does not have a condition that excludes them	Gratz (2001), Rossi et al. (1999), Tveskov and Angelo-Nielsen (1993), Talmar et al. (2006) and White (2004a)
<i>Setting</i>	
Ensure the treatment environment is safe	Campbell and Hopwood (2004) and White (2004a)
<i>Risk reduction</i>	
Discuss benefits of supervised self-treatment	Yamashita et al. (2001)
Ensure the area to be needled is anatomically safe	Campbell and Hopwood (2004) and Peuker (2004)
Avoid (anatomically) 'forbidden points', e.g. the nipple or the umbilicus	Peuker et al. (1999)
Treat 'low-risk', easily reached areas	Teig et al. (2006)
Stress the importance of depth of needle insertion	Lee et al. (2005), Peuker (2004), Stack (1975), White (2004a) and Willims (1991)
Ensure use of single use disposable needles	Hayhoe et al. (2002)
Discuss the increased risk of breakage with fine needles	Hayhoe et al. (2002)
Discuss the use of guide tubes	Kobayashi et al. (2010)
Acupuncturists who self-needle should follow the same advice as other patients and avoid risk	Yamashita et al. (2001)
<i>Professional activities</i>	
Knowledge of anatomy aids safety	Rampes and James (1995) and White (2004a).
Have a working knowledge of anatomy and revisit anatomy regularly as part of rigorous training curricula, regulation and continuing professional development (CPD)	Peuker and Cummings (2003), Peuker et al. (1999) and White (2004a)
Ensure communications between all carers in primary and secondary care	Priddle and Forrester (2007)
<i>Managing complications</i>	
Discuss how to manage an accidentally broken needle	Campbell and Hopwood (2004); Murata et al. (1990); Rampes and James (1995); Yamashita et al. (2001).
<i>Contraindications and precautions</i>	
Arrange safe needle disposal	Filshie (2003), Priddle and Forrester (2007) and White (2004a)
Discuss the need to report symptom and/or efficacy change	Campbell (2001)
There may be special considerations in pregnancy	Forrester (2003), Smith et al. (2002) and White (2004a)
Special precautions for patient with diabetes and those who are immunocompromised or on anticoagulant medication	Shah et al. (2002) and White (2004a) White (2004a)
Discuss special considerations for electroacupuncture	Smith et al. (1986) and White (2004a) Murata et al. (1990), White (2004a) and Cummings (2011)

## Training

On the whole, patients and their caregivers are quick to learn the skills needed for effective SHA. Most will have mastered the skills of needle handling and point location in two or three training sessions (Cheville and Basford, 2006), and some will only need one session to be able to needle safely. These students of SHA are often healthcare workers or have had previous experience of needle usage, either injections or electrolysis in beauty therapy (Dyer et al., 2013). Patients can use their mobile phones to take pictures of the needles in situ to aid future practice.

There may also be a role for acupuncture organisations to debate the issues of definition of SHA, development of consensus SHA practice guidelines and questions for further research. Haas et al. (2013) concluded from one chronic disease perspective, 'Evidence suggests that the development of standardised procedures for documentation, training health professionals to document appropriately, and the use of structured standardised forms based on current practice guidelines can improve documentation and may ultimately improve quality of care'. The same conclusion applies to the practice of SHA.

## Cost savings

In a typical health service setting, SHA should reduce costs to the service in the management of long term conditions as a result of reduced attendance at clinics, both in primary and secondary care, thus increasing capacity.

In the paying healthcare sector, SHA will reduce revenue to the therapist due to fewer clinic attendances, but also reduce costs to the patient through fewer appointment sessions and less travel time and time off work, offset by the cost of equipment (needles, sharps box, EA machines).

In most practices (Dyer et al., 2013; Walter and Curtis, 2013), the patient would be expected to buy their own equipment for their own ongoing SHA.

As Molassiotis (2013) says: 'it makes more financial sense in healthcare systems to focus on reducing costs and minimising unnecessary access to treatment and therapists'.

## Effectiveness

SHA may only be an elaborate healing ritual '*performed by a patient or patient's acupuncture partner*' (Dyer et al., 2013), but it can have profound therapeutic effects (Dyer et al., 2013; Walter and Curtis, 2013) and, perhaps in the same way as therapist applied acupuncture, involves modulation of symptoms through neurobiological mechanisms (Kaptchuk, 2011).

Clinical experience suggests that SHA is just as effective as therapist acupuncture in many situations. Patients do not seem to notice any reduction in therapeutic effect when they or their caregiver deliver the acupuncture rather than the acupuncturist (Dyer et al., 2013; Walter and Curtis, 2013). The therapeutic relationship is important and powerful in acupuncture, but this is not lost when engaging in SHA, and it could be argued that, in fact, it grows in the process through empowering the patient/caregiver.

## Continuing management

Campbell (Campbell and Hopwood, 2004) relates his experiences that some patients find SHA not quite as good as therapist acupuncture and come back for an occasional top-up. He postulates that there may be something extra that is being contributed by the therapist (Campbell, 2000). Hopwood emphasised the lack of treatment flexibility: 'If the same points are treated at every session, it is an indication of poor acupuncture' (p. 143) and stressed the importance of the therapeutic relationship between acupuncturist and patient, and skilled therapeutic hands,

as safety imperatives. Filshie (personal communication) agrees that some clinic treatments, e.g. three monthly, may be needed to maximise the response, perhaps by permitting a higher dose of acupuncture. Furthermore, clinic follow-up may be needed for treatment of less accessible points or needling areas that require special precautions such as the chest wall.

To reduce the need for regular out-patient or GP follow up, follow up may be implemented with texts, email, FaceTime/Skype (Video call) (Walter and Curtis, 2013), using security appropriate to the clinical setting, or communication by post. Peer group support could be coordinated in a manner similar to the National Cancer Survivorship Initiative (National Cancer Survivorship Initiative, 2013).

## Legal aspects

Some therapists have been concerned that their medical defence body may not cover them, in respect of SHA. It seems likely that a 'body of opinion of practising acupuncturists' supports the principle of SHA, and the fact that the patient/caregiver has been adequately trained in SHA would show a duty of care. Good record keeping and the existence of appropriate protocols for the procedure would also be best practice (Campbell and Hopwood, 2004).

In some cases, acupuncturists may need to check that their professional body's Codes of Professional Conduct permits teaching patients self-needling techniques, which is likely to be necessary for indemnity insurance cover.

## Concluding comments

SHA may only be an elaborate healing ritual with profound therapeutic effects, probably involving modulation of symptoms through neurobiological mechanisms in the same way as therapist applied acupuncture.

SHA seems safe and acceptable to patients and many acupuncturists. There is a huge unmet need of acupuncture in areas such as cancer survivorship, chronic pain self-management, mental health, palliative care and functional disorders, which can be met by self-care in this way.

Formal guidelines should be developed for individual settings based on those already published. Supervision and support are needed, both for teachers and for patients/caregivers. These can be arranged locally, with appropriately agreed guidelines. The use of SHA is surrounded by obstacles such as risk, that can be managed in an intelligent way, prejudices and conflicts of interest. If these could be overcome, SHA could become routine acupuncture practice which will undoubtedly be in the best interests of our patients.

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# Integration of acupuncture in the health service

S. Hayhoe ■ A. White and Contributors

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## Introduction

This chapter reports several examples of acupuncture integrated within conventional health care, either as part of everyday practice or in a dedicated clinic (for ease, ‘clinic’ is used for both situations). These examples were chosen simply for convenience, and many other clinics exist in different countries, specialties and settings.

One of the aims of this chapter is to highlight how the experience of acupuncture clinics contributes to the total evidence base for acupuncture’s effectiveness in health care. Acupuncture clinics are usually founded by champions who, convinced of acupuncture’s benefit to patients, enthusiastically implement their vision, sometimes having to overcome a degree of opposition. This is a common story with innovations in health care before they gain widespread acceptance. Personal reports of the benefits of acupuncture spread through social networks and establish a clinic’s good reputation and thus its continued existence or expansion. Sometimes the demand can even be overwhelming. Individual clinic audits provide an additional level of more formal evidence (e.g. Ross, 2001; Blossfeldt, 2004; Day and Kingsbury-Smith, 2004; Freedman, 2002; Harborow and Ogden, 2004; Rosted et al., 2006).

*‘Evidence based medicine... integrates the best external evidence with individual clinical expertise and patients’ choice’*

(Sackett et al., 1996).

The evidence of successful results in practice from clinics where acupuncture is integrated may formally be classified only as anecdote and observation, but it augments and complements the more theoretical clinical research at higher levels. Thus, for musculoskeletal medicine, robust evidence from meta-analysis of 29 high quality RCTs shows that acupuncture is more effective than

sham for various painful conditions (Vickers et al., 2012) and rigorous network meta-analysis of RCTs of conservative treatments for knee osteoarthritis including 25 acupuncture trials shows acupuncture to be one of the most effective (Corbett et al., 2013). These formal studies finally validate the consistent reports over many years of successful treatment in musculoskeletal clinics where acupuncture is provided. The combination of evidence and experience is convincing. Moreover, it seems that where anecdote and careful clinical observation lead, clinical research eventually follows, and it is likely that evidence for at least some other conditions will follow the same process and eventually paint a similarly coherent picture.

While this chapter focuses on patient benefit from integrated acupuncture, it also aims to highlight other advantages: potential cost savings; job satisfaction for practitioners; and the opportunity to expand the body of knowledge about acupuncture and its applications, which can be achieved by reporting clinical observations, whether positive or negative, honestly, for the benefit of patients and practitioners. Case histories and audits may stand low in the hierarchy of evidence, but careful observation opens the pathway that leads ultimately to the definitive randomised, pragmatic trials.

The use of acupuncture for a particular patient is based, often in the absence of adequate evidence, on the clinician's judgement and the patient's wish, but in a few conditions acupuncture is recommended by national guidelines such as those of NICE in the UK for back pain (NICE [CG88], 2009) and headache (NICE [CG150], 2012) and the German Ministry of Health for back pain and knee osteoarthritis (Cummings, 2009). Although acupuncture is a relatively low-cost resource and has long been popular with patients (Hayhoe, 1981), practitioners note that flexible, enlightened administrators and management are crucial for success in the setting up and running of clinics.

## Primary care

The logistics of primary care consultation and funding vary considerably between different countries, which will have a major influence on the ability to offer acupuncture. In some countries patients expect general practitioners to offer at least one complementary therapy, often acupuncture, as an integrated part of their practice. In the UK, there is still a degree of scepticism about acupuncture from the more conservative elements of the medical profession, and a lack of appreciation of the growing evidence base for its effectiveness in a range of conditions. Indeed, Wye et al. (2009a) found that although the majority of clinicians and managers claimed research evidence guided their decisions on complementary therapies, their behaviour appeared to be based on perception of evidence rather than factual knowledge. Time is also seen as an increasingly scarce resource in primary care, so spending time on acupuncture may be criticised as time away from frontline work, or even as self-indulgence.

Successful integration of acupuncture therefore requires efforts to promote its understanding and acceptance both informally and at educational meetings, particularly to explain the conditions that are likely to respond to treatment. Patients help by reporting success with acupuncture to other doctors and patients, and these stories inevitably filter through the medical fraternity so that confidence in acupuncture grows.

*Satisfying for practitioner: but I love acupuncture fresh to the episode, not as a stale regimented course far far away in pain clinics.*

Jens Foell, GP.

Many GPs/family practitioners integrate acupuncture within their daily work – but acupuncture has to fit the constraints of primary care, not vice versa. For example, in UK practice a standard appointment time of 10 min allows for only brief needling which, with one or two

follow-up treatments, can still be successful in treating a range of acute, painful, mainly musculoskeletal conditions (Freedman, 2002). One UK general practice uses its website to promote information about acupuncture services: this speeds the consultation process, is cheaper than printed leaflets and can be updated more easily. Once oral consent has been obtained and the needles are in, the remaining time can be used to deal with other matters, such as health promotion. Patients are discharged once a reasonable response is obtained, but have the option of returning for further treatment if necessary.

Patients who need long-term treatment (e.g. migraine, chronic pain from advanced arthritis, irritable bowel and premenstrual syndromes) are seen every 4–8 weeks in a dedicated weekly acupuncture clinic, using up to four rooms and jointly staffed by a practice nurse. The same clinic is used for patients with acute problems needing more than the two or three appointments available in normal appointment time; in this case further follow up is available on demand, arranged by phone call to the doctor. This acupuncture clinic is partially supported by voluntary donation, with an amount of £15 per treatment suggested on a notice in public view, though never directly requested from patients (Freedman and Richardson, 2005). This has proved an acceptable method of covering costs in the UK, but health service funding remains problematic here as in many countries. In Australia reimbursement for acupuncture is often at a lower level than a standard consultation, so GPs have taken to referring patients to third party (often physiotherapist) acupuncturists for treatment, or alternatively claim for ‘dry needling’ which perversely attracts the standard fee (Wardle et al., 2013).

## GROUP CLINICS

Access to one GP weekly acupuncture clinic in London (UK) is mainly by referral and not widely advertised, but to meet demand it is held in a large room with two couches, one massage chair and three optional chairs, so four patients can be treated with overlapping appointments at 10 min intervals, avoiding mixing of sexes. A neighbouring room is available but can add the risk of forgetting a patient who is out of sight. The use of rooms and screens is flexible, so barriers for sight are possible but not for sound. This can hinder personal assessment and goal setting, but allows some group interaction. There is almost no limit to the conditions treated although myofascial pain predominates, and the clinic particularly targets patients who are unresponsive to other treatments or psychologically distressed. Patients may return as necessary but, since this is primary care, discharging is difficult, although if patients do not respond in three sessions, consensual reassessment is necessary; patients rarely abuse the facility.

Long-term conditions need long-term maintenance treatment. In order to provide this economically, another UK practice treats six to eight patients with osteoarthritis of the knee together in one room. The first consultation is held individually to allow history taking and examination, and thereafter treatment is given as a group. The fund-holders were persuaded that money could be saved by offering on-going acupuncture to patients instead of surgical referral and possible knee replacement. This nurse-led clinic, run over two sites, has been highly successful, and even makes a small profit. It is very popular with patients who enjoy the social interaction and self-help tips suggested by others in the group (Asprey et al., 2012). Although minimal skin exposure is required for standard electroacupuncture to the knee, single sex groups are preferred. Acupuncture is accepted by 84% of patients referred, and after 2 years 30% could be identified that had continued using acupuncture and not had surgery. Using realistic assumptions, the cost consequences for the local commissioning group are an estimated saving of £100 000 a year (White et al., 2012).

*Well, it was quite nice being in the group. Because you kind of think, well other people have got the same sort of problems, you're not completely weird!*

Knee clinic patient (Asprey et al., 2012).

## COSTS AND FUNDING

Reviewing the database of a Dutch national insurer of 1.5 million patients, [Baars and Kooreman \(2014\)](#) found that those with a GP trained in a complementary therapy had significantly reduced health care costs (by 10%) mainly due to lower hospital and pharmacy charges. This has long been the observation of individual UK GPs using acupuncture ([Downey, 1995; Lindall, 1999](#)). So integrating acupuncture into general practice is likely to prove cost-effective and, in a review of service audits, [Wye et al. \(2009b\)](#) found primary care complementary therapy services to be clinically effective with a ‘moderate to strong impact on health status scores’.

In the UK, most dedicated general practice acupuncture clinics are charity or patient funded ([Luff and Thomas, 1999](#)) or involve creative use of existing resources (e.g. ancillary staff budget) since setting up a clinic with health service funding can be frustratingly slow and fraught with difficulty. [Wye et al. \(2008\)](#), after investigating funded clinics, produced a model for a clinic that meets the needs of the health service (but not necessarily those of patient or practice) ([Figure 13.1](#)). The model specifies that treatment should be restricted to conditions where evidence exists and other treatments are ineffective, should target high priority populations, aim to reduce overall health service costs (perhaps by avoiding surgery as in the knee clinic above) and avoid addressing the ‘unmet need’ of patients currently managing outside the health system. The service should be limited to a specific number of treatments per person, and referrals should be tightly regulated to avoid over demand. The practitioners (doctors, nurses or physiotherapists) must be appropriately trained and skilled in acupuncture, and regular audit must demonstrate safety and continuing

### Specific therapies for specific conditions

Chosen on basis that:

- Perception treatment works
- Little available in biomedicine

### NHS management priorities

- Populations with high health need
- Reduces NHS cost pressures
- Does not pick up unmet need
- Controls on patient demand

### Other service features

- Regular evaluation
- Affordable
- Well-advertised
- Trained and registered therapists
- Personal contact between therapists and referrers
- Limited numbers of therapists and referrers
- Referrers observe consultations
- Doctors as therapists

**Figure 13.1** Service model characteristics of a ‘NHS friendly’ complementary therapy service. (Reproduced from [Wye, L., Shaw, A., Sharp, D., 2008. Designing a ‘NHS friendly’ complementary therapy service: a qualitative case study. BMC Health Serv. Res. 8, 173 \(under Creative Commons\).](#))

clinical and financial effectiveness. A business plan compliant with these challenging requirements offers a reasonable chance of being funded (Lim, 2010), but still depends on persuading fund-holders.

*I think any introduction of complementary therapies has to be incredibly disciplined. And so we need very clear protocols that say this is the sort of case, this is the sort of need that we're going to meet through this service. Not a 'come all ye'.*

PCT (fund-holder) manager (Wye et al., 2008).

There is a contradiction between this model, with referrals limited by the requirements of health policy, and the way most GPs would choose to organise acupuncture for greatest benefit, which is to include patients with conditions, mostly musculoskeletal, of recent onset, often too recent to establish a clear diagnosis. These conditions, almost impossible to define adequately for clinical research, are anecdotally probably the most responsive of all applications of acupuncture. Further, GPs are uniquely qualified to identify patients with psychological difficulties such as anxiety and adverse reactions to stress and to apply acupuncture to promote sleep, alter perception of pain and improve that nebulous aspect 'quality of life', allowing the patient to resume a more normal life pattern.

Unfortunately, clinics relying on conventional funding are susceptible to politically imposed financial constraints. In the UK there have been a number of clinics, both in general practice and hospital, where funding was withdrawn during periods of monetary restraint. Despite this, a limited acupuncture service has often survived through the use of one or more of the strategies reported in this chapter, or simply by giving acupuncture treatment, albeit briefly, during normal consultation time.

## Secondary care

The provision of acupuncture in specialist hospital departments may be simpler than in primary care. Few, apart from chronic pain management, will need a dedicated acupuncture clinic, and most consultants will have sufficient autonomy to provide whatever immediate service is appropriate to their patients, particularly if it is inexpensive in itself and appears cost-effective in terms of patient satisfaction and avoidance of more costly procedures. Specialist consultations tend to be flexible, providing time to integrate minor treatment such as acupuncture. The common out-patient format of consulting room and one or more satellite rooms with examination couch and facilities for treatment is very suitable. There, after insertion of needles, a patient can be left in the treatment room, possibly undergoing electroacupuncture, in the care of the clinic nurse while the specialist engages with another patient in the consulting room.

Acupuncture may be appropriate only for a limited proportion of patients, depending on the specialty, but then provides a good chance of rapid benefit. However, as patients may not come with any expectation of acupuncture, it is important to provide information and obtain (and record) consent to treatment to forestall objection to the sudden imposition of needling, particularly if treatment proves unsuccessful.

Examples of specialist departments where acupuncture has been successfully integrated on a regular basis include; rheumatology (Alexander and White, 2000), orthopaedic, neurology, cancer and palliative care (Filshie and Hester, 2006), paediatric cancer, geriatrics (Warne, 2002), ear, nose and throat, emergency medicine (Zhang et al., 2014), respiratory, dermatology (Iliev, 1994), gynaecology and obstetrics (Selva Olid et al., 2013), smoking cessation services (Chang et al., 2013) and drug rehabilitation (Cui et al., 2013). In many areas of medicine the traditional role of doctors has been augmented or even taken over by specialist nurses or physician assistants. This is

already happening with acupuncture in individual departments where the use of semi-formulaic traditional or trigger point acupuncture for specific problems allows effective treatment within a limited area of expertise. An example of this is the obstetric use of acupuncture by midwives.

## OBSTETRICS IN SWEDISH HOSPITALS

Western medical acupuncture was approved by the Swedish National Board of Health and Welfare in 1984 to be used by licensed health personnel – initially for chronic pain only, but since 1993 for any condition with evidence of effectiveness. Nonetheless acupuncture remains mostly used by physiotherapists treating pain conditions in primary care or, less commonly, in hospitals.

The use of acupuncture in obstetrics has changed over time. Swedish midwives adopted it with enthusiasm, attending courses of 3–4 days at their hospital's expense and applying it within their normal practice: in the antenatal period for hyperemesis and pelvic instability, in labour for retained placenta as well as for pain and relaxation, and after delivery for post-labour pains, milk stasis and urinary retention (Martensson et al., 2011a). Nearly a quarter of women used acupuncture for labour pains in the 1990s. However, the figure fell to 6% in 2011, probably because enthusiasm was unmatched by rigour of training and application. The reasons behind this fall are instructive: training courses are not standardised and often have little academic content (Martensson et al., 2011b), continuing education is largely absent, and guidelines have been poorly drawn with inadequate details for best practice (Schytt et al., 2011).

## PHYSIOTHERAPY

Most physiotherapy departments offer acupuncture; indeed this is a perfect example of true integration. Where deemed appropriate, acupuncture is used together with stretches, manipulation, soft tissue massage, re-education of movement, and exercises for a wide variety of musculoskeletal disorders. In addition patients with chronic pain benefit from acupuncture offered alongside pain education programmes. The advantage in physiotherapy is that acupuncture can provide useful, non-drug analgesia, facilitating the all-important exercises. It also improves local blood flow, which takes away irritant metabolites of exercise, and helps to relax muscles so that they can be more fully stretched, allowing greater mobility of affected joints and potential for improved quality of movement control in the affected region. Not surprisingly this proves popular with physiotherapists and patients alike. The acupuncture is performed very much as part of routine treatment in the normal circumstances of any busy physiotherapy department, usually a large room with several physiotherapists operating in curtained cubicles. No special arrangements need be made for the use of acupuncture.

*I think this is a particular strength of Western medical practitioners using acupuncture integrated within the overall management plan for a patient, so that the most useful combination of interventions is selected by practitioners with expertise in their own discipline but also with access to a multidisciplinary team full of expertise.*

Clare Donnellan, Neuro-physiotherapist.

The physiotherapy department within a large UK university teaching hospital illustrates the integration of acupuncture throughout the entire department. Management of pain is the main indication, but the usefulness of acupuncture for influencing issues such as low mood, anxiety and sleep dysfunction is recognised and valued. Staff within the musculoskeletal teams including chronic pain management and occupational health physiotherapy use acupuncture, as do physiotherapists in the palliative care team and within the amputee service for management of stump and phantom limb pain. But a particularly novel and successful area is neuro-rehabilitation.

Physiotherapists provide acupuncture right across the rehabilitation pathway: both in- and out-patient units, and in the community outreach therapy teams. Conditions regularly treated include: traumatic brain injury, spinal injury, resected brain or spinal tumour, Guillain-Barré syndrome, hereditary spastic paraparesis, multiple sclerosis (Karparkin et al., 2014), Parkinson's disease (Zeng et al., 2013), later stage stroke (Lim et al., 2015; Wu et al., 2010) and metastatic spinal cord compression. Acupuncture is helpful in managing many of the associated symptoms such as pain, nausea, poor sleep and fatigue, relief of which can aid patients' engagement in treatments to improve sitting and standing balance, mobility and independence in daily activities. Also a calmer, more relaxed patient with less pain may participate more effectively with the speech therapist or psychologist.

Initially the consultants and other members of the multidisciplinary team had no idea whether acupuncture would be useful, but agreed that a simple and inexpensive intervention would be welcomed if it provided some good results. Positive feedback from patients, often during ward rounds, rapidly demonstrated that it was a useful option and now referrals from the out-patient clinics and requests from patients themselves have become standard. When it seems that acupuncture might help a new patient, this is discussed with their rehabilitation medicine consultant and other members of the team, highlighting any special issues such as ability to consent if the patient has aphasia or information from the occupational therapist regarding perceptual or cognitive issues which might influence treatment. On nearly all occasions the decision is to go ahead, but discussion allows broader understanding of potential issues and involves all of the multidisciplinary team in the decision to use acupuncture as a formal part of the treatment plan.

The advantage of this set-up is that acupuncture is truly integrated within a range of options, including pharmacological, medical and physical re-education treatments. A disadvantage is that in times of staff shortage, acupuncture treatments may need to be temporarily omitted. The regularity of a dedicated acupuncture clinic might ensure consistency of acupuncture provision but does not offer the flexibility, benefits and likely synergism that the integrated approach of multiple treatment modes can provide.

## Palliative care

Acupuncture is provided in 59% of hospices (Leng 2012). Clinics are sometimes launched by patient request, one example being the regular weekly acupuncture clinic in a UK Hospice. Most consultations are in out-patients, a few in day care or inpatients. Referrals are from GPs, hospital consultants or Macmillan (cancer) nurses. Staffing consists of a consultant and a specialist physiotherapist (who also uses acupuncture on home visits). Nurses have their own roles including undertaking the monthly changes of indwelling needles used for symptoms such as breathlessness – where it was found that sternal needles achieved 50% success (Bausewein et al., 2008).

Patients undergo conventional palliative care and continue their medical treatment whilst having acupuncture. Current medication is maintained, but often fewer doses of breakthrough analgesic are needed, even if regular analgesia remains unchanged – although in some cases this can gradually be reduced too. Patients undergoing active treatment such as chemotherapy or radiotherapy can also receive acupuncture, though indwelling needles are not used in patients at risk of neutropenia.

Experience suggests that acupuncture is particularly useful for patients with residual symptoms despite conventional medication, such as nausea and vomiting and also for conditions where conventional treatment is lacking, such as dry mouth, myofascial pain and neuropathic pain, including chemotherapy induced peripheral neuropathy. Good results are seen in both men (prostate cancer) and women (breast and gynaecological cancer) with hot flushes and sweating from hormone therapy, some showing a dramatic improvement in symptoms following acupuncture, thus avoiding the need to stop the hormone treatment. This group of patients seems particularly

suitable for self acupuncture at home (Filshie et al., 2005; Filshie and Hester, 2006; also see Chapter 34) as they often have good prognosis and are relatively well but require regular, ongoing acupuncture.

An unpublished audit of 100 consecutive patients at the hospice showed that roughly two-thirds of patients with pain and half with non-pain symptoms reported a good or excellent response to acupuncture. Myofascial pain (Baldry, 2004), joint pain and scar pain (Fang, 2014) improved in the majority of patients and better responses were observed when symptoms were not directly due to the underlying disease but were unrelated or a result of treatment.

## Tertiary care – pain clinic

Hospital acupuncture clinics can very easily be swamped by referrals, causing an excessively long waiting list. This is not only unacceptable for patients waiting in pain, but reduces the chance of success if pain becomes more intractable. One solution is to accept referrals only from other hospital departments, or even just from other members of the pain team. This restriction is unfortunate, but offers the chance to educate the referrers and reduce inappropriate referrals to a minimum. With a long waiting list, there is a problem that by the time their first appointment comes round some patients will have forgotten or will no longer need treatment. Telephone or text reminders reduce the number failing to attend.

Normally appointments are made well in advance, so a booked series of six should avoid interrupted treatment. This does lack flexibility, but with a regular course there is chance to gain maximum pain relief, build up rapport with patients and provide the education and psychological support that is so helpful when suffering chronic pain. However, this type of consultation is time consuming and labour intensive, as although little time is needed for needle insertion and removal, about 20 min is necessary for EA or 10 min for manual stimulation. Appointments will thus usually last between 20 and 30 min. An alternative is for the acupuncturist to work in association with the clinic nurse, allowing several patients to be treated at the same time. Evidence suggests this has no detrimental effect on clinical outcome but does reduce waiting-list time (Berkovitz et al., 2008) and is, of course, more cost-effective.

*This patient was absolutely delighted with the results, her only complaint being “Why was this not offered 17 years ago?”*

Shanti Rajan, Medical Acupuncturist, Pain Clinic (Rajan, 1999).

Fitting in extra sessions after an initial treatment course can interrupt the regular sequence of appointments for other patients, extending the waiting list still further but nonetheless leaving unfilled clinic places. So it may be necessary to limit treatments to (e.g.) six booked appointments per patient, at the end of which, if suitable, they might be taught self-needling to use at home (Campbell and Hopwood, 2004; Teig et al., 2006; also see Chapter 12) or else they must make arrangements for treatment elsewhere: in primary care or privately, if they feel that possible additional benefit warrants the expense. This rule should improve waiting times considerably, but introduces the ethical and legal difficulty of what to recommend for patients after they have been discharged from a hospital, or indeed any other limited medical acupuncture clinic.

Legally the situation on referral varies from country to country (Gilmour et al., 2011a,b), but in general formal referral can be made only to a practitioner who is regulated by a statutory body (e.g. Registered Physiotherapist). In this case, provided he has the appropriate expertise, he can take over responsibility for care of the patient. Referral or recommendation to an unregulated therapist may be regarded as delegation, where the therapist is actually providing treatment ‘on your behalf’, in which case you could be considered vicariously liable for any negligence of the therapist unless you have confirmed his adequate training and experience (GMC, 2006).

Beyond this, there remains the ethical responsibility of ensuring that your patients come to no harm by having treatment from unqualified practitioners. Thus, if you suggest that they find their own acupuncturist through a business directory or friend's recommendation, you should give advice concerning what training, form of practice and membership of national acupuncture associations would be appropriate in a therapist likely to offer safe practice conditions.

## Outsourcing

In Nottingham (UK) the hospital pain clinic acupuncture service was put out to tender in 2008 and is currently provided by three community based providers, one of which is a private acupuncture company run by nurses. Access to the acupuncture clinic is by direct GP referral with a tariff set by the purchasing organisation. Moving the service to a private provider in the community has resulted in savings per treatment of around 40%. Cost saving is not the only reason for outsourcing: the referral pathway is simpler, it reduces the need for a chronic pain specialist appointment, and is quicker and more convenient for the patient. The team is able to provide a local service to patients at seven health care centres throughout the city (other teams offer a further three locations), clinics are arranged to suit working patients with early morning and evening appointments, and top-up sessions can be continued on demand for up to a year following their initial course of six. Discharging patients after a year prevents blocking of clinic places and ensures a sustainable service.

The clinics use two rooms close to each other, so two patients can be seen at a time with appointments of 45–50 min including 30 min of treatment. Administration includes electronic referral, contacting patients for booking and regular feedback of treatment and results to the GP. A text reminder service, along with a strict policy of cancellation for nonattenders, keeps the no-show rate down to less than 5% (around 10% for hospital clinics).

Approximately 500 new patients are seen a year and audit has shown a 98% overall satisfaction with the service. The majority of referrals are for low back pain, but headaches, neck and shoulder pain, knee pain and fibromyalgia are also treated regularly. The more that success is reported back by patients to their GP, the more referrals are made, but advance planning is problematic as the contract needs renewal annually, so an uncertain future makes employing additional staff or planning expansion difficult.

## Key Points

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### Summary points: benefits of acupuncture integration

- Integrated acupuncture is popular with patients.
  - Acupuncture can sometimes be effective where other treatments have failed.
  - Acupuncture treatment can be offered immediately, at a first visit.
  - Acupuncture can be used as a clinical trial when the diagnosis is unclear.
  - Acupuncture can be used as part of an overall treatment plan.
  - Acupuncture may reduce the need for secondary referral.
  - Acupuncture can be provided with minimal cost and administration.
  - Acupuncture may easily be combined with other modes of medical treatment.
  - Integration gives great scope for innovation and observation.
  - Integration of acupuncture offers a high degree of clinician satisfaction.
- 

## Concluding comments

The integration of acupuncture into hospital and general practice is popular with patients, and appears to provide a clinically and economically effective service, though not appreciated enough managerially to generate regular funding. Nonetheless the high level of satisfaction that clinicians experience suggests that the effort to achieve integration is well rewarded by seeing patients benefit.

One clear theme is evident in the earlier examples: there is increasing reliance on nurses and physiotherapists for the provision of integrated acupuncture within health services. Though unwelcome to some doctors who have pioneered medical acupuncture and striven to make it acceptable to their colleagues, the change is inevitable, both economically and practically, but must be accompanied by the promotion of high quality medical acupuncture training courses.

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# Safety of acupuncture

A. White ■ M. Cummings

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## Introduction

Unquestionably, acupuncture is a very safe treatment indeed in the hands of properly trained practitioners. With millions of treatments given globally each year, serious adverse events (AEs) are very rarely reported, although minor, self-limiting events are relatively common.

Patients are increasingly demanding treatments that are safe; indeed they may seek acupuncture for its reputation for being safe. It causes less harm globally than some drugs used for similar conditions, such as non-steroidal anti-inflammatory drugs (NSAIDs). A few AEs are unavoidable, but training and careful practice reduce the incidence to a minimum. The problem is complacency: safe practice requires a culture of safety to prevail throughout the whole profession and a positive approach by individual practitioners.

Clinical points

‘A fool learns from his own mistakes. The wise man learns from the mistakes of others.’  
Otto von Bismarck.

This chapter aims to enable safer practice by selecting relevant literature. Early reports of safety were summarised (White, 2004), and several systematic reviews have been published since (Zhang et al., 2010; Vohra et al., 2011; He et al., 2012; Zheng et al., 2012; Xu et al., 2013). This chapter does intend to cause alarm, but does not shrink from describing some of the serious AEs, including deaths, where they provide important learning points. The chapter is practical and does not claim to be comprehensive.

Table 14.1 presents a self-checklist, illustrating that acupuncture cannot be practised safely without a knowledge of medicine – diagnosis, prevention and treatment – which is assumed here. Systematic advice on safer practice is available elsewhere (White et al., 2008).

After discussing evidence, attribution and incidence, this chapter will describe AEs in relevant categories, followed by remarks on particular acupuncture techniques and on patients in whom additional care is required. Standard definitions of terms used are given in Table 14.2.

EVIDENCE AND ATTRIBUTION

Before describing incidence of AEs, we describe problems in establishing the evidence.

Case reports describe AEs, but provide no information on incidence. Such anecdotes can be dramatic and may generate alarmist media headlines out of all proportion to the likelihood of their being repeated (Kmietowicz, 2012). Prospective surveys provide reasonably accurate estimates of incidence, but have limitations: underreporting (e.g. by practitioners, to protect themselves),

TABLE 14.1 ■ List of self-check questions for safe acupuncture practise

Knowledge domain	Self-check question
Acupuncture	Is this patient particularly vulnerable for any reason?
Medicine	Should this patient be having acupuncture, or is a different treatment indicated?
Acupuncture	Do I know exactly which tissues this needle will penetrate?
Acupuncture	Does this particular technique carry any added risk, for example, electroacupuncture (EA)?
Medicine	Is infection control technique compromised in any way?
Administration	Is all my equipment of highest quality and good condition?
Medicine	Can I diagnose and manage any AEs, including referral if necessary?

TABLE 14.2 ■ Standard safety terminology used in this chapter

Term	Definition
Adverse event (AE)	Any untoward occurrence during or after treatment with acupuncture
Serious AEs	Those that lead to death, hospital admission or prolonged stay, or result in persistent disability or incapacity, or are life threatening
Attribution, causality	An AE may occur after acupuncture but not be correctly attributed to it. See text for tests of attribution
Adverse reaction	An event definitely caused by acupuncture May be unavoidable or avoidable

overreporting (e.g. patients with low reporting threshold) and risk of errors from misunderstanding of definitions, misreporting and so on.

'Secondary' reports, typically surveys asking health care staff what AEs they can recall associated with acupuncture, are less reliable. Clinical trials usually provide little useful data on safety as they are too small to provide data for rare events.

The relationship between the AE and any treatment (attribution) can be classified as certain; probable/likely; possible; unlikely; and unclassifiable. AEs can rarely be attributed to acupuncture with 'certainty': this requires that the time relation is plausible, a possible mechanism is available, and no better explanation available (Edwards and Aronson, 2000). The acid test of certainty is whether the event recurs when the intervention is repeated, which in the case of acupuncture is not usually advisable clinically or permissible ethically. However, in one case from Denmark, a 22-year-old woman with asthma was treated for dermatitis and 1 h later experienced an asthma attack. This recurred each time she was treated. On the fourth occasion it was so severe that acupuncture was abandoned (Rosted, 1996). Fortunately her dermatitis had resolved.

The most unequivocal evidence of 'certain' causality by acupuncture is the discovery of the needle, e.g. on imaging or surgical exploration.

Unfortunately, serious medical incidents may be falsely attributed to acupuncture in order to discredit it. In some cases, acupuncture was given for early symptoms of the condition that was already developing. A typical feature of such reports is that authors do not investigate and report precise details of the acupuncture given, which are needed to establish attribution.

## INCIDENCE OF AEs

Nine early surveys collected data from Czechoslovakia, Germany, Japan, Singapore, Sweden and Taipei (Ernst and White, 2001). The most serious events were two cases of pneumothorax and two of broken needles requiring surgical removal. Frequency of AEs varied between surveys, for reasons to be discussed.

A prospective survey of 31 822 acupuncture consultations with 78 doctors and physiotherapists in the United Kingdom reported an overall AE incidence of 6.8% of consultations (White et al., 2001a,b). No AE was serious, but 13 interfered with daily activities, such as drowsiness or hyperaesthesia. One patient suffered a convulsion, discussed in the succeeding text. Avoidable events included forgotten patients, needles left in patients or cellulitis after needling an area of lymphoedema and moxa burns. A similar study of 34 000 consultations with non-medically trained practitioners had very similar results (MacPherson et al., 2001).

A total of 13 579 German physicians recorded AEs on 229 230 patients each receiving an average of 10 acupuncture treatments – approximately 2.2 million sessions (Witt et al., 2009). The overall AE rate was 8.6%, over half of which were bleeding; 2.2% of patients experienced an event that required some form of treatment from the practitioner – mostly, pressure to stop bleeding. Two patients suffered pneumothorax, one of whom required hospital admission. The longest lasting event – 180 days – was a nerve injury in the lower limb. AEs that indicated any degree of negligence amounted to 0.1% of the total. The data from this study are presented in Box 14.1 as indicative of the safety of acupuncture.

Acupuncture is used at various locations in the British National Health Service (NHS), and, like all treatments, is monitored by reporting of AEs to a national register. In a 2-year period, the register received 3.7 million patient safety reports of which 325 involved acupuncture (Whewy et al., 2012). These events included 59 incidents where patients found needles left in place after treatment; 41 incidents where the patient was 'forgotten' in a cubicle and treated longer than intended; 99 incidents of dizziness or faintness without loss of consciousness and 63 with temporary loss of consciousness. Eight patients fell off the couch during or immediately after treatment, and four fell down outside the clinic after treatment. There were seven incidents of bruising or

**BOX 14.1 ■ Classified incidence of adverse events recorded by physicians as associated with 2.2 million people treated with acupuncture (Witt et al., 2009)**

**Common incidence: from 1:10 to 1:100**

- Bleeding including haematoma

**Uncommon incidence: from 1:100 to 1:1000**

- Inflammation, swelling or pain at needle site
- Local muscle pain
- Nerve irritation or injury
- Headache, fatigue, vertigo and nausea

**Rare: from 1:1000 to 1:10000**

- Local infection, redness and itching
- Sweating
- Autonomic symptoms including increase or decrease in BP, tachycardia, breathing difficulties
- Vomiting
- Worsening health state, generalised muscle pain, restricted movement and joint problems
- Feelings of coldness, depressed mood, anxiety, sleep disturbance, restlessness/nervousness, disturbed vision, tinnitus and unconsciousness
- Menstrual problems

**Very rare: <1:10000**

- Palpitations, constipation, diarrhoea, gastrospasm, enterospasm and circulatory disturbance
- Weight loss
- Lesion of blood vessels
- Systemic infection
- Euphoria, nightmares, poor concentration, imbalance, speech disturbance, disorientation and shivering
- Eye irritation
- Forgotten or broken needle
- Pneumothorax; injuries to other organs

*Data based on 2 million consultations (Witt et al., 2009).*

soreness at the needle site and one of small blisters. There were five possible incidents of pneumothorax of which two were confirmed diagnoses; one was classified as 'severe.' The authors commented that acupuncture 'seems to be a low harm treatment.' However, there is clearly room for improving the administrative aspect of treatment.

In summary, there is good evidence that acupuncture is a safe treatment, with an incidence of serious AEs (e.g. pneumothorax) of <1/10 000, which is classified as very rare. The most common AE is bleeding.

## Minor events

Minor events are in themselves self-limiting, but may lead to more serious complications such as drowsiness that may cause accidents.

## BLEEDING

Occasional bleeding from small vessels cannot be avoided, and the reported rate is highly variable, the average for typical clinical practise being 3–6% (Witt et al., 2009). The reported rate will depend on whether it was the patient or the practitioner reporting, and the precise definition

used. The style of acupuncture and setting can play a part: particularly high rates were reported in a clinical trial in dental patients (List and Helkimo, 1992). Frequency also depends on location of needling: treatment of facial points may more commonly result in haematomas that are exposed and therefore more visible.

## NEEDLE PAIN

Needle pain is common in some settings: this refers to sharp pain, not *de qi*, which has dull, spreading characteristics though is sometimes described as ‘painful.’ Needle pain was reported between 0.2% and 13% in normal practise, and a typical average is about 1% (White et al., 2001a). Quality of needle manufacture can contribute to pain. Electron micrograph examination of needle tips show that some of them are hooked (Hayhoe et al., 2002; Xie et al., 2014).

## SYMPTOM EXACERBATION

Exacerbation of symptoms also occurs in about 1% of consultations. Anecdotally, exacerbation is more likely with more intensive needle stimulation.

## SYNCOPE

Feelings of faintness during needling occur between 0.3% and 0.7% of consultations (White et al., 2001a; Witt et al., 2009). Full syncope (generally when the patient is upright) brings the risk of anoxic convulsion. A fit 25-year-old man was having his first acupuncture treatment for shoulder pain, in a sitting position to allow access (Hayhoe, 1987). Needles were inserted lightly into his neck and shoulder, then finally into LI4 where manipulation elicited *de qi*. The patient said he felt faint, and while being placed supine he stiffened and had a grand mal seizure with urinary incontinence. He occupied the couch all morning while recovering and felt ill for a week.

### Clinical points

Patients should be treated on a couch, ideally lying, especially first time. Patients who are treated sitting for any reason should be observed carefully and laid supine if feeling at all faint.

## DROWSINESS

Lethargy and drowsiness are common during and after treatment, in up to 12% of patients (MacPherson et al., 2001). One study reported that about a third of 122 consecutive patients treated for pain were excessively drowsy immediately after acupuncture and were considered at significant risk of road traffic accidents (Brattberg, 1986).

### Clinical points

Patients should be warned not to drive after acupuncture until they are sure they are not affected by drowsiness.

## SKIN AND SUBCUTANEOUS TISSUE

Reports of skin problems with acupuncture are rather rare. Pigmentation of the needle puncture sites has been reported after manual and electroacupuncture (Miao, 2011). Local inflammation around the needled site occurs in about 0.3% (Witt et al., 2009). A 23-year-old oriental woman with a known diagnosis of psoriasis developed six guttate, scaling lesions 2–4cm diameter symmetrically down alongside the spine after treatment with a ‘seven star silver’ needle 3 months

earlier (Kirschbaum, 1972). Other examples of the Koebner phenomenon have been reported (Wu and Caperton, 2013; Zhu et al., 2011).

A 55-year-old Japanese woman developed match-head sized papules at the site of acupuncture needle insertion (Yanagihara et al., 2000). After biopsy, papules again developed in biopsy sites. Samples showed granulomatous lesions with giant cells containing silicone, and the diagnosis was silicone granuloma, which may be a delayed type hypersensitivity.

An otherwise healthy 59-year-old woman had acupuncture several times over 1 year for a sprained ankle. She developed 2–5 mm granulomatous lesions at the needling sites, again a reaction to the silicone coating on the needles (Alani and Busam, 2001).

An eruption of lichen planus started at the points used in acupuncture for back pain in a 41-year-old woman and rapidly spread to involve the whole body except face, palms and soles (Fleming et al., 2011). Two other acupuncturists reported pyoderma gangrenosum and lichen planus attributed to immune responses to acupuncture (Xu et al., 2013). Two cases were reported of lipatrophy in the site of acupuncture needling, as may be seen after injection of drugs (Drago et al., 1996). They resolved over a year. Two cases of factitial panniculitis have been reported after multiple electroacupuncture sessions for weight loss (Jeong and Lee, 2009).

OTHER SELF-LIMITING AEs

The comprehensive German study reported many other AEs (Witt et al., 2009), though the attribution of some might be questioned. Headaches were one of the more common, as high as 0.5%, followed by nausea, vomiting and vertigo, which were classified as uncommon ( $\geq 1/1000$  to  $\leq 1/100$ ). Sweating is rarely reported, though it can be marked.

Very occasionally, an individual report appears which suggests an individualistic response. For example, female patients have experienced galactorrhoea following acupuncture (Campbell and Macglashan, 2005; Jenner and Filshie, 2002). A case of nystagmus was reported (Bradbury et al., 2006).

Clinical points

Most deaths and serious injuries attributed to acupuncture are caused by trauma.

Trauma

Virtually every organ in the human body has been pierced, to the serious detriment of its owner, by an acupuncture needle. In some cases, the needle was too long or inserted in the wrong place; in others, a needle inserted elsewhere has broken and migrated. Trauma has to be regarded as avoidable in at least 90% of cases; an exception might be perforation of an anomalous artery. No acupuncturist should ever proceed with a needle insertion until he or she has answered the question (see Table 14.1: ‘Do I know exactly which tissues this needle will penetrate?’).

The points needled in 26 traumatic fatalities reported from China from 1956 to 2010 are presented in Table 14.3 (He et al., 2012). Relatively few were caused by trained acupuncturists, most

TABLE 14.3 ■ Point locations incriminated in fatal complications of acupuncture in China, He et al., 2012 (cases, if >1)

Location	Points
Neck	GB20 (6), GV16 (3), ST9, LI17
Shoulder area	GB21 (3), tender point
Sternal area and epigastrium	CV22, xiphisternum, CV15
Back and chest	BL13 (2), tender points (4), LR14

by barefoot doctors – and some were related to needling directly through clothing (*sic*). Nine other deaths were caused by infection. The main errors in technique were described as:

- needling too deep
- not locating the point accurately
- movement of the patient during treatment
- using too strong electrical stimulation.

Many serious AEs present in emergency wards, and patients may be reluctant (or in no physical condition) to report having acupuncture; emergency medical staff need to be alert to a possibility of acupuncture trauma.

## PNEUMOTHORAX

Pneumothorax is the most common serious AE and the most common cause of fatality from acupuncture.

### Clinical points

Pneumothorax is avoidable. Practitioners needling the thorax should choose points wisely; insert either over a rib, at a tangent to the ribcage or in a shallow oblique direction.

Early reports of pneumothorax happened when needling over the ribs or at the root of the neck. But later, pneumothorax was more likely when treating upper back pain, using spinal and paraspinal points (Xu et al., 2013). These cases were often bilateral. Note that the pleurae extend close to the spinal column.

Symptoms of pneumothorax may develop slowly over 48 h, but occasionally are devastatingly swift and give little time for life-saving treatment. A 72-year-old woman, weighing 53.3 kg, had regular treatment for neck and back pain. On the day in question, 20–30 needles were inserted over the back, and when they were removed, she complained of chest pain and dyspnoea which rapidly worsened (Iwadate et al., 2003). Taken straight to hospital, she was found to be in cardio-pulmonary arrest and died within 90 min of the onset of symptoms. At post mortem examination, several ecchymoses were seen on the parietal pleura alongside the spine.

There is little room for error in depth of needling for thin, emaciated patients, though there is also a risk in needling overweight or obese patients as it can be difficult to judge the actual depth of a needle in relation to the thicker tissue layers.

## HEART

Cardiac tamponade can develop with similar catastrophic speed. A 40-year-old Norwegian woman being treated for fibromyalgia was needled at CV17 (Halvorsen et al., 1995). She experienced immediate chest pain and an overwhelming feeling of death; she collapsed and was pronounced dead on arrival at hospital within 2 h. In this case the needle tip passed through a foramen in the lower sternum, an anatomical variant that occurs in 5–8% of the population (Peuker and Cummings, 2003). Rarer anomalies, such as sternal clefts, may also pose a risk when performing acupuncture in this area (Toso et al., 2012).

A 62-year-old man had a branch of the right coronary artery ‘shredded’ by a sub-sternal acupuncture needle (Her et al., 2013). After resuscitation of cardiac arrest, he required cardiac bypass surgery for ligation of the damaged artery. He recovered fully.

The heart and pericardium are vulnerable to any needling over the anterior chest wall, sternum and epigastrium. Widespread publicity has been given to the sternal foramen and its variations (Toso et al., 2012; Travan, 2012). But needles inserted elsewhere can migrate and lodge in the heart; at open heart surgery, two needles were found in the interventricular septum of a 49-year-old woman who had been treated by an acupuncturist in Korea for bilateral shoulder pain

(Ernst and Zhang, 2011). In that case it was not clear whether the needles were left *in situ* intentionally, but in other cases embedded needles have migrated to the heart, particularly from the neck and shoulders (Xu et al., 2013). Despite these warnings, direct injuries to the heart still occur: the same review found five cases in 10 years.

### Clinical points

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Needles inserted over the precordium must not penetrate deeper than the surface of sternum or ribcage.

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## MAJOR VESSELS

A 43-year-old Australian man developed sudden onset calf pain and swelling behind the knee while sitting down (Lord and Schwartz, 1996). He had been needled at BL40 several weeks previously for back pain. The correct diagnosis eluded hospital staff for 1 month despite repeated attendance and investigation. Finally at exploratory surgery, 800 mL blood was removed and pseudoaneurysm was diagnosed. The authors suggest that the needle penetrating a vessel wall caused a haematoma which then organised but remained connected to the vessel lumen, forming a pseudoaneurysm. This remained silent until ruptured presumably by the minor trauma of hitting the chair during sitting down.

Pseudoaneurysms from acupuncture have been reported alongside the abdominal aorta. It is the popliteal artery that is vulnerable at the back of knee, with several reports of aneurysms and an arteriovenous fistula (White, 2004).

A patient treated for back pain with an abdominal insertion of a needle described as 150 mm long (*sic*) developed an aortoduodenal fistula causing a massive haematemesis from which he died 2 weeks after acupuncture (Chang et al., 2005).

### Clinical points

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Needling into the abdominal cavity should be avoided.

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## OTHER BLOOD VESSELS

Haemorrhage may occur from smaller arteries almost anywhere in the body, may be serious and may cause diagnostic difficulties.

One woman aged 37 years was admitted 4 h after acupuncture with abdominal pain and vomiting and was eventually diagnosed only after CT scan: needles had penetrated the epigastric artery causing a large haematoma in the rectus sheath (Cheng and Liu, 2005). It resolved over 1 month without specific treatment. A similar case in a 71-year-old woman was resolved by catheterisation of the artery and embolisation with cyanoacrylate glue (Moon et al., 2013).

A 72-year-old Japanese woman was admitted as an emergency after collapsing with a large retroperitoneal mass involving the kidney (Matsuyama and Nagao, 1998). Earlier that day, she had acupuncture in the renal region for lumbar pain, and needles had penetrated the kidney tissue causing haemorrhage.

A 44-year-old Chinese man presented with severe headache, nausea and vomiting that started during needling of GV16 for neck pain (Choo and Yue, 2000). He had signs of meningism, lumbar puncture revealed blood in the cerebrospinal fluid (CSF) and computerised tomography (CT) scan showed haemorrhage in the fourth, third and lateral ventricles.

Thirty-five cases of subarachnoid haemorrhage and spinal epidural haematoma were found in the Chinese literature (Zhang et al., 2010). The points most frequently involved were GB20, GV15, GV16, GV14 and BL10. In several cases, the needles were inserted to a depth of 4–5 cm, which is likely to be deep enough to reach the epidural space in the midline of some smaller patients.

Arterial bleeding in a closed compartment compresses other tissues, sometimes dangerously. Immediately after acupuncture near GB34, a 68-year-old man experienced shin pain which

gradually worsened with swelling and discolouration (Smith et al., 1986). He was admitted to hospital on the fifth day, and surgical decompression saved the leg.

A 69-year-old man developed weakness of arms and legs from a subdural haematoma 2 h after acupuncture in the neck (Park et al., 2013). Initially it was assumed he had a transient ischaemic attack. He fully recovered normal function after surgical decompression.

Needling even the most commonly used point, LI4, can cause significant haemorrhage from the palmar metacarpal artery. Deep needling should be avoided, and Wong (2013) reported that LI4's location is given differently in different texts, and distal locations are likely to be safer than proximal.

## BRAIN, SPINAL CORD AND MENINGES

The brain and spinal cord can be affected by trauma to the blood supply (in the preceding text), by infection (described in the succeeding text) and by penetration by an acupuncture needle (White, 2004; Xu et al., 2013). This can occur directly during treatment, or from migration of broken needles or embedded needles, sometimes many years later. Injury has been reported to the spinal cord, causing transverse myelopathy (Ilhan et al., 1995); to medulla oblongata; and even to the cerebellum. Surgery may be necessary to remove needle fragments, and such patients may not recover normal sensation (Xu et al., 2013).

One 47-year-old Japanese man needled himself in the neck over many years for headaches and neck stiffness (Miyamoto et al., 2010). One day the needle broke and he reported to hospital: the needle was removed surgically with considerable difficulty having embedded itself in the medulla and cerebellum. A middle-aged woman inserted a sewing needle to treat her neck and could not remove it; it was removed surgically (Anderson and Datta, 2007).

Spinal cord penetration usually presents with sensory symptoms or motor weakness. But one patient presented with urinary retention, which resolved with surgical removal of a needle from C1/2 (Gi et al., 1994).

## PERIPHERAL NERVE

Experiments with ultrasound imaging show that an acupuncture needle can penetrate the median nerve without causing any symptoms apart from the slight ache of *de qi* (Kessler and Streitberger, 2008). This supports the traditional explanation of why nerve injury is quite rare – the needle point parts the nerve bundle fibres but does not cut them. However, peroneal palsy and drop foot have been reported (White, 2004), and Xu et al. found reports of injuries to peroneal nerve (GB34), facial nerve (ST7, ST8) and median nerve (PC5, PC6), as well as the L5 nerve root from a broken needle in the lumbar region (Xu et al., 2013).

## OTHER LOCATIONS

After treatment of the back, pneumoretroperitoneum has been reported (Hwang et al., 2008).

Two days after acupuncture for her knee pain, a 72-year-old lady presented with a tender, swollen and red painful leg (Gray, 1996). With a provisional diagnosis of deep vein thrombosis she was started on anti-coagulant drugs while awaiting imaging – which showed the needle had ruptured a Baker's cyst.

Five articles reported six injuries to the eyes in China, including orbital haemorrhage (3), traumatic cataract (1), injury of the oculomotor nerve (1) and retinal puncture (1). One case of optic atrophy accompanied by haemorrhage and traumatic cataract resulted in visual impairment (Zhang et al., 2010). The points used in the earlier cases were BL1, Qihou (EX-HN7) and ST1. The orbital cavity is vascular, so bleeding is difficult to avoid, even for the experienced acupuncturist, and deep needling can also injure the oculomotor nerve, the retina and neighbouring tissues. These dangers are described in Chapter 30.

Clinical points

Needling into the orbit should only be undertaken by eye specialists.

Tissue and organ infection

LOCALISED

Infections associated with acupuncture appear to be increasing in line with the increased rate of infections occurring in other forms of health care (Xu et al., 2013). Many cases, particularly the more serious ones, have an element of chance or idiosyncrasy and can be considered unavoidable. But all reports serve as a reminder to screen patients for increased susceptibility. Cases of localised infection reported from 2000 to 2011 from many different countries and involving many different organs have been categorised (Table 14.4).

The most serious local infections are those that develop into necrotising fasciitis, with its 20–30% mortality. Deaths have been reported (White, 2004), though none were found in a subsequent review (Xu et al., 2013).

Clinical points

Needles should not be inserted through skin that is affected by any pathology.

TABLE 14.4 ■ Details of local infections categorised by location of treatment

Location treated	Diagnosis: organism (n = cases)
Ear	Cellulitis: <i>Pseudomonas aeruginosa</i> (1) unknown (2)
Knee joint	Septic arthritis: <i>Mycobacterium chelonae</i> (1) <i>Staphylococcus aureus</i> (1) MRSA <sup>a</sup> (1) <i>Listeria monocytogenes</i> (1) <i>Streptococcus faecalis</i> (1) from embedded needles unknown (1 <sup>b</sup> )
Spinal column	Septic arthritis: MRSA (1) Unknown (2) Discitis: <i>Staphylococcus</i> (1)
Low back	Pneumoretroperitoneum (1), unclear whether infected or not Psoas abscess: unknown (1) Other paraspinal soft tissues: <i>Escherichia coli</i> (1) MRSA (1)
Skin	Facial erysipelas: unknown (1) Other sites: <i>Mycobacterium</i> (various spp) (7)
Various other soft tissue	Cellulitis or abscess: <i>Staphylococcus aureus</i> (3) unknown (3 – 2 <sup>b</sup> , 1 > osteomyelitis) <i>Klebsiella pneumoniae</i> (1)
Abdomen	Intra-abdominal abscess (1)
Shoulder	Pleural empyema (1)
Calf	Tendonitis: <i>Streptococcus</i> (1)
Other	Subperiosteal abscess of frontal bone (Pott's puffy tumour) (1)

<sup>a</sup>MRSA: methicillin-resistant *Staphylococcus aureus*.

<sup>b</sup>Developed necrotising fasciitis.

Source: Xu et al. (2013).

Communications must be good between all those caring for any patients who may be at particular risk because of immune status or blood conditions. One patient died from organ failure complicating a localised infection of the leg after acupuncture given by his general practitioner, who had not been informed by the hospital that the patient had developed pancytopenia (Simmons, 2006).

### Clinical points

Practitioners should be aware that muscle tenderness can be due to preexisting infection.

The source of infection may be the practitioner. Many cases of *Mycobacterium* skin infection were reported at clinics in Korea; in one clinic, they were traced to improper sterilisation of towels and packs placed on acupuncture points after the needles were withdrawn, and in another clinic to improper preparation of the fluid used to clean the skin (Xu et al., 2013).

Sporadic cases of *Staphylococcal* infection are frequently reported, but a series of eight cases due to methicillin-resistant organisms were traced to a practitioner who was a carrier of the same clone that infected patients (Murray et al., 2008).

Psoas abscess after acupuncture has been reported. However, psoas abscess usually occurs spontaneously, and since acupuncture was given for back pain, it seems at least possible that the developing abscess came before the acupuncture (White and Cummings, 2009).

Occasional reports are seen of sacroiliitis (Lau et al., 1998; Tseng et al., 2014).

## ENDOCARDITIS

Eight case reports of endocarditis after acupuncture were found in an earlier review (White, 2004), including one infection of a prosthetic valve. In 2011, another case of endocarditis occurred in a child aged 15 with severe eczema who abandoned conventional medical treatment and was treated by acupuncture: needles were reportedly inserted into the inflamed skin around the knees and the puncture sites firmly massaged afterwards (Buckley, 2011). Two days after the fifth treatment he developed bilateral knee swelling and fever, and after admission to hospital his condition deteriorated and endocarditis was diagnosed with infected emboli and empyema in the lungs. *Staphylococcus aureus* was cultured from blood.

### Clinical points

When using acupuncture in patients with damaged heart valves, use clinically clean technique and avoid inflamed or abnormal skin; reported cases of endocarditis involve an element of chance or idiosyncrasy.

## CHONDRITIS AND PERICHONDRITIS

The ear is worth special mention, as it is particularly vulnerable to infection and a common site for acupuncture. Auricular infection was the second most common infection after hepatitis (White, 2004). Infection may require surgical intervention and may cause permanent deformity of the pinna.

Indwelling needles, as foreign bodies, represent the major infection risk. In view of the risk that they may fall out and spread hepatitis or HIV, it is wise always to use indwelling needles that are easily visible and firmly stuck to the dressing.

## MENINGES, BRAIN AND SPINAL CORD

These tissues are the site of occasional infection after any kind of needling: a survey found eight cases in which purulent meningitis or spinal abscess was associated with epidural, paradural or facet joint injection of pharmacological agents for back pain (Gaul et al., 2005).

An 80-year-old woman presented with 2 days of progressive quadriparesis, difficulty voiding urine, and fever (Yu et al., 2013). She had received acupuncture for spinal problems on 5 days in the previous week. MRI showed multiple epidural abscesses at C3–C7, L3–5 and L5–S1 from which *S. aureus* was isolated.

The vital sense organs, integral with the central nervous system, are vulnerable. A 67-year-old Chinese man developed an epidural abscess between the second and sixth cervical vertebrae after receiving acupuncture (Lee and Chee, 2002). He was toxic on admission to hospital and the following day suddenly lost the vision of his left eye from extension of the infection to the vitreous humour. Despite intensive antibiotic therapy and surgery, the sight could not be saved, though he had no other residual neurological deficit.

## Generalised (systemic) infection

Generalised infections include viral communicable diseases and opportunistic bacterial infections, mainly from inoculation of the patient's own pathogenic flora.

### HEPATITIS

Hepatitis B used to be the most common serious AE reported with acupuncture, with 94 cases in four outbreaks caused by contaminated needles identified in a literature review in 2003 (Lao et al., 2003). Ten years later, the same researchers could find no new reports (Xu et al., 2013), which they attributed to the widespread introduction of single-use disposable needles. Yet it has to be recognised that chronic hepatitis B infection due originally to acupuncture remains a public health problem, as identified in rural Vietnam (Nguyen et al., 2007) and in the elderly in Brazil (de Paula Machado et al., 2013). The significance of hepatitis is the risk of progression to cirrhosis and hepatocellular carcinoma.

Epidemiological studies, more reliable indicators of incidence than case reports, suggest that hepatitis may still be being caused by acupuncture in certain geographic regions or particular populations. In the American Asian population, acupuncture was a significant risk factor for hepatitis C, second only in frequency to blood transfusion (Kin et al., 2013). A significant association between acupuncture and hepatitis C was also reported from Chengdu, China (He et al., 2011) but was not found in Korea (Seong et al., 2013).

### Clinical points

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A global drive for single-use disposable needles is needed. Acupuncturists should be immunised against hepatitis B because of the risk of acquiring infection via needle-stick injury or even a drop of blood onto any tiny breach in the skin.

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### HIV/ACQUIRED IMMUNE DEFICIENCY SYNDROME

Four cases of HIV transmission were reported in association with acupuncture, the last known in 2003 (White, 2004). A case in Thailand seems certainly to have been caused by shared acupuncture needles with no sterilisation. Patients treated with reused needles are clearly at risk.

### SEPTICAEMIA

Sepsis at a site remote from the acupuncture is one of the most difficult conditions to be sure of attribution. A 48-year-old woman was admitted to hospital with infection in the shoulder region and small lesion in the foot, which the patient said was one site where she had been needled for chronic fatigue syndrome (Maas et al., 2013). *S. aureus* was cultured from the blood, and she responded to flucloxacillin. There is no doubt that acupuncture has caused septicaemia in some vulnerable patients (Pierik, 1982). Injection needles carry a similar risk of occasional, idiosyncratic sepsis.

## PREVENTION OF INFECTION

Bacterial infections seem most likely to have occurred through the introduction of the patient's own skin contaminants (White, 2004). This is clearly shown in the case of endocarditis (Buckley, 2011).

Complete sterilisation of the skin is not even possible under surgical conditions, which are totally impracticable for acupuncture practise anyway (Hoffman, 2001). The accidental inoculation of external organisms from the practitioner's hands is unlikely but possible, since in practise acupuncture is a 'clean' rather than a 'sterile' procedure. However, the number of organisms that can be inoculated by a needle tip is unlikely to be sufficient to cause local infection, and infection is rarely reported after acupuncture.

There may be a higher risk of infection under certain circumstances such as diabetes, immunosuppression, or neutropenia, but local or regional factors may also be relevant, such as lymphoedema (Dupuy et al., 1999) or the presence of implants near the skin surface (Laing et al., 2002). In the latter circumstances the position of needling can be altered to minimise the risk of infection.

### Clinical points

Practitioners need to remain alert for the possible risk factors or infection, including the site needled (joint spaces, meninges, ears and around implants) and the susceptibility of the patient (immunosuppression, heart valve disease).

## Miscellaneous

### LOSS OF CONSCIOUSNESS AND CONVULSIONS

Convulsions occurring during syncope were discussed earlier, but various events associated with altered level of consciousness have also been described.

One man aged 35 suffered a seizure during treatment in the prone position for back pain (White et al., 2001a). Needles were inserted 1 cm deep in his hands, back muscles and feet. They were not stimulated and did not cause pain. Within a few minutes, the patient developed a strong flexor spasm of the whole body and became unconscious. He was unconscious for about 3 min, then recovered complaining of nausea and fatigue. He had bitten his tongue. On further questioning, he gave a history of one previous seizure during a painful cystoscopy. He had subsequently donated blood with only a transient feeling of faintness. The diagnosis may have been reflex anoxic seizure.

A patient experienced impaired consciousness 34 h after the first treatment with acupuncture and again during the second session (Beable, 2013). He had a history of idiopathic complex partial seizures which had been controlled, as well as occasional undiagnosed 'unusual events.' At his second treatment, shortly after needling the calf muscle, he reported abnormal sensations and loss of muscle power then became unresponsive for several minutes, eventually recovering fully after 50 min. The author comments that acupuncture, cataplexy and complex partial seizures may involve similar neurological pathways. She commented that the patient's history was not initially sufficient to deny him acupuncture, but the report of 'vague staring episodes' 4 h after the first treatment could be regarded as reason to have abandoned treatment.

### OTHER

A 26-year-old woman presented with neck pain 2 months after acupuncture, which had caused some swelling (Lee et al., 2013). Myositis ossificans was diagnosed after biopsy of the paraspinal muscles. The patient gradually recovered without treatment.

## Acupuncture tools and techniques

### EQUIPMENT

Needle quality has improved over time but must not be compromised by cost savings. Needle breakage, now rarely reported, creates a foreign body that must be removed. The handles of some early disposable needles came loose as they were not properly attached to the shafts. Electron microscopy has shown loose bodies (Hayhoe et al., 2002; Xie et al., 2014) in both Chinese and Japanese needles widely available for purchase. Metals adherent to or contaminating the stainless steel can cause contact dermatitis.

The output of EA apparatus must meet its stated specifications at all frequencies and intensities, which was not true of three machines in one test (Lytle et al., 2000). It is a wise precaution to have individual machines tested, for example by the local hospital physics department. Further, the wave form and current produced by some machines are capable of causing macroscopic tissue damage.

Special equipment may carry special risks: a ‘small needle knife’ Xiaozendao, reported to be widely used in traditional settings in Asian countries, has a flat cutting edge. Part of one broke off in the neck and lay dormant for 3 years, gradually migrating to the epidural space causing neck pain and upper limb neuropathy until removed surgically (Liou et al., 2007).

### ELECTROACUPUNCTURE

The risk, precautions and AEs of electroacupuncture are described in [Chapter 11](#).

### MOXIBUSTION

Moxibustion can cause burns that may result in scars. Those most commonly reported in the literature are the result of carelessness suggesting the need to develop clear safety routines. Scarring is sometimes induced intentionally as a form of treatment.

### RETAINED NEEDLES

A former treatment technique, now outlawed in Japan, involved inserting the needle subcutaneously and cutting off the handle (okibari). Needles are still seen in x-ray images subcutaneously where they were left, but more seriously they have repeatedly been shown to have migrated to, and often severely damaged, distant tissues, including the heart (Hasegawa et al., 1991; Kataoka, 1997), medulla oblongata, peritoneal cavity, liver, colon and bladder (Gerard et al., 1995).

Other cases of ‘retained’ needle occur because the needle broke during treatment and was ignored.

### Clinical points

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Every broken needle should be considered for surgical removal.

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The risks of auricular chondritis and perichondritis were discussed earlier.

Another form of sustained stimulation involves the insertion of catgut sutures, which have been blamed for psoas abscess leading to aortic aneurysm (Origuchi et al., 2000).

### MISCELLANEOUS

Self-acupuncture constitutes increased risk, so careful training and supervision are essential (see [Chapter 12](#)). Self-acupuncture of the heart with a sewing needle by an unqualified practitioner was fatal (Schiff, 1965). Several other cases of self-penetration of the heart have been

recorded, either accidental or associated with self-mutilation (Keogh et al., 1988), suicide attempts or mental disorder (Dwivedi et al., 1991), but not believed to be associated in any way with acupuncture.

Trauma through self-needling of the neck was reported earlier (trauma to brain and spinal cord).

Needling for pain relief after fracture risks converting a closed fracture into the much more dangerous open type (Kelsey, 1998).

## Patients at particular risk

A 44-year-old woman who jogged regularly developed calf pain. She had a single treatment with acupuncture, the skin being prepared with an alcohol swab, and 2 days later developed redness, swelling and fever and was subsequently admitted to hospital with disproportionate pain. The infection progressed and necrotising fasciitis of *Staphylococcal* origin diagnosed by her rapid deterioration and the imaging appearance of deep oedema and fluid. She responded eventually to conservative treatment. The patient had not said she had aplastic anaemia – and the acupuncturist had not asked (Hsieh et al., 2011).

A 78-year-old man had four semi-permanent needles inserted for postoperative pain control; fluid replacement was such that he developed dilutional thrombocytopenia and consequently haematoma on the ear as well as operation site (Usichenko et al., 2006).

Cardiomegaly presents an increased risk of direct cardiac injury (Zhang et al., 2010).

History of convulsions as a risk factor for acupuncture is discussed earlier.

Patients with peripheral neuropathy are vulnerable to burns with moxibustion.

## PAEDIATRIC ACUPUNCTURE

A total of 279 AEs in children were identified, 25 of them serious (Vohra et al., 2011). There were 12 cases of thumb deformity reported from a Chinese clinic from 1983 to 1989, most if not all after treatment at LI4. Nine had fibrosis of the thenar muscle, and the other three were fibrotic changes; all had corrective surgery. There were five cases of infection: HIV (described later), septic sacroiliitis, septic arthritis of a lumbar facet joint, pyogenic spondylitis of the thoracic spine, and Pott's puffy tumour (subperiosteal abscess) of the frontal bone.

A 9-year-old boy in China, already seriously ill with pulmonary TB and heart disease, died from cardiac rupture from acupuncture needles inserted through his clothing. A 15-year-old French girl had a pneumothorax after acupuncture. A case from 1984 reported a 16-year-old Japanese boy with fatigue in whom 70 needles were implanted, one of which lodged in the cervical spine causing muscle weakness and sensory loss. Strength returned after surgery but the sensory loss continued. An 11-year-old Chinese girl had a traumatic subarachnoid haemorrhage: she was being treated for speech disorders, and a needle had been inserted deeply (2 in., 5 cm) just above the thyroid cartilage.

A Chinese boy aged 2 years with diarrhoea was treated with abdominal acupuncture, after which he deteriorated with intestinal obstruction. Exploratory surgery revealed a haematoma obstructing the intestine; after it was resected, he recovered fully. A child in a vegetative state had haemoptysis after acupuncture, and an X-ray image revealed a needle inhaled through his tracheostomy. It was removed surgically. A 15-year-old Canadian boy was unrousable after treatment with acupuncture lying on his side; he recovered spontaneously after 2 h, but the event was repeated on the next treatment. He was subsequently shown to have posterior cerebral hypoperfusion, and symptoms were attributed to his position during treatment rather than the treatment itself.

Data from randomised controlled trials in children suggests an AE rate of about 12% (Vohra et al., 2011).

## Concluding comments

Reports of AEs after acupuncture should not detract from the basic message that it is a very safe therapy in the hands of trained practitioners. Safety depends on the quality of initial training and of repeated updating throughout a lifetime of practise. But avoidable events occur, so attention needs to be paid to even better quality procedures (observing patients, counting needles in and out), better knowledge of anatomy and microbiology, increased awareness of the risks and repeated attention to infection control. Practitioners must be willing and able to deal adequately with the AEs that they encounter, including knowing when it is appropriate to request assistance.

Patients vary in how much information they want about the risks of treatment and should be informed appropriately.

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## *Related techniques*

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# Transcutaneous electrical nerve stimulation (TENS)

M.I. Johnson ■ J.W. Thompson<sup>†</sup>

## CHAPTER OUTLINE

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## Historical background

From time immemorial it has been known that when a part of the human body becomes painful it is an intuitive response to stroke, massage or rub the affected part because this tends to relieve the pain. In other words, local stimulation interferes somehow with the perception of pain. When a pain is very severe it may require very intense stimulation, to the extent of producing its own pain, before the original pain is reduced to any useful degree. It is common knowledge that electrical currents can excite nerves in the skin and influence the activity of other tissues of the body. The use of electricity for therapeutic purposes (electrotherapy) and especially for the relief of pain (electroanalgesia) also originates in antiquity, as evidenced by stone carvings which date from the Egyptian Fifth Dynasty (*c.*, 2500 BC) and show the use of the electric fish (*Malapterurus electricus*) to treat painful conditions (Gildenberg, 2006). Over 2000 years later Hippocrates (400 BC) referred to the use of the electric torpedo fish for the treatment of such conditions as headache and arthritis. Other techniques have been used as a means of stimulating the skin for the relief of various painful conditions including heat packs, ice, laser, massage, manipulation and mobilisation, vibration, ultrasound and acupuncture. All these foregoing methods are examples of stimulation-induced analgesia. Electroanalgesia is convenient to apply and the different parameters of stimulation are simple to control.

<sup>†</sup>Deceased.

ELECTROANALGESIA

There has been continuous interest and development in electroanalgesia over the last four and a half thousand years (Table 15.1). Up to the twentieth century, progress was concerned mainly with identifying those conditions which responded to electroanalgesia and also to developments of the apparatus used to apply electrotherapy. A pivotal point in the history of electrotherapy occurred in 1965 when Melzack and Wall proposed their Gate Control Theory of pain which, in essence, stated that the input of pain information to the brain was controlled at spinal cord level by a gate mechanism which was itself influenced by the nature and intensity of non-painful information entering the spinal cord (Melzack and Wall, 1965). This hypothesis was readily verifiable and was soon put to the test by Wall and Sweet (1967) when they showed that high frequency (50–100 Hz) percutaneous electrical nerve stimulation relieved chronic neurogenic pain (Wall and Sweet, 1967). In the same year, Shealy and his colleagues performed the first dorsal column implantation and were able to show that electrical stimulation of the dorsal column was also effective for the relief of chronic pain (Shealy et al., 1967). In 1969, Reynolds made a discovery of fundamental importance (although not recognised so at the time), namely that electrical stimulation of the periaqueductal grey (PAG) area of the rat brain produced surgical anaesthesia (Reynolds, 1969). In the meantime, transcutaneous electrical nerve stimulation (TENS) was being utilised to select patients for dorsal column implantation. But it was soon realised by Long and his associates that TENS alone was often effective in relieving chronic pain and thus largely obviated the need for patients to undergo an operation for dorsal column implantation (Long et al., 1973; Long et al., 1979).

In theory, it is possible to stimulate electrically any part of the nervous system, but in practice it has been found that pain relief occurs only when specific parts are stimulated, and this applies in particular to the relief of chronic pain (Table 15.2). Electrical stimulation of a main sensory nerve or some of its cutaneous branches which innervate a painful part of the body may produce pain relief in the same way as rubbing a painful part. This may be achieved using electrodes attached to the intact surface of the skin (i.e. TENS) or using electrodes inserted through the skin (e.g. electroacupuncture and percutaneous electrical nerve stimulation). Implanting electrodes in the epidural space to stimulate the spinal cord (i.e. spinal cord stimulation) and in the thalamus and

TABLE 15.1 ■ Some milestones in electroanalgesia

2500BC	Egyptian fifth dynasty	Stone carvings show electric fish <i>Malapterurus electricus</i> used to treat painful conditions
400BC	Hippocrates	Used electric fish to treat headache and arthritis
1759	Dr. John Wesley	In <i>Electricity made plain and useful by a lover of mankind and of common sense</i> he described treatment of sciatica, headache, gout, kidney stone, etc.
1965	R. Melzack and P. Wall	Proposed the Gate Control Theory of Pain
1967	P. Wall and W. Sweet	Reported use of high frequency (50–100 Hz) percutaneous electrical nerve stimulation for relief of chronic neurogenic (neuropathic) pain
1967	C.N. Shealy et al.	Reported use of dorsal column stimulation of spinal cord
1969	D.V. Reynolds	Discovered that stimulation of periaqueductal grey (PAG) in the midbrain of rat produces surgical anaesthesia
1973	D.M. Long	Reported results of transcutaneous electrical nerve stimulation (TENS)
1979	M.B.E. Eriksson and B. Sjölund	Reported increased analgesic benefit of acupuncture-like TENS (AL-TENS) compared with conventional TENS

TABLE 15.2 ■ Sites and methods of electrical stimulation used to relieve pain

Division of nervous system	Anatomical area	Method of electrical stimulation
Peripheral nerve	Cutaneous	Transcutaneous (TENS, TENS-like devices) Percutaneous Electroacupuncture
	Nerve trunk	Transcutaneous (TENS, TENS-like devices) Percutaneous Implanted electrodes
Spinal cord	Dorsal column	Implanted electrodes Percutaneously introduced electrical stimulation of the spinal cord
Brain	Thalamus (posterior ventrolateral nucleus)	Implanted electrodes
	Periventricular grey matter	Implanted electrodes
	Other sites	Implanted electrodes

the periventricular grey matter (i.e. deep brain stimulation) have been shown to relieve ischaemic and neuropathic pain and are used to relieve intractable pain which has failed to respond to other methods of pain relief (Hamani et al., 2006; Simpson and Stannard, 2005). More recently, non-invasive techniques have been used to stimulate the brain for pain relief with evidence that using transcranial magnetic stimulation of the motor cortex may produce short-term analgesia (O’Connell et al., 2010).

Principles of TENS

Any technique that delivers electricity across the intact surface of the skin to activate underlying nerves is, strictly speaking, TENS (Johnson, 2014). However, healthcare professionals use the term TENS to describe the use of portable battery-powered machines producing pulsed electrical currents up to 60 milliamperes (mA) in amplitude to relieve pain (Fig. 15.1; Box 15.1).

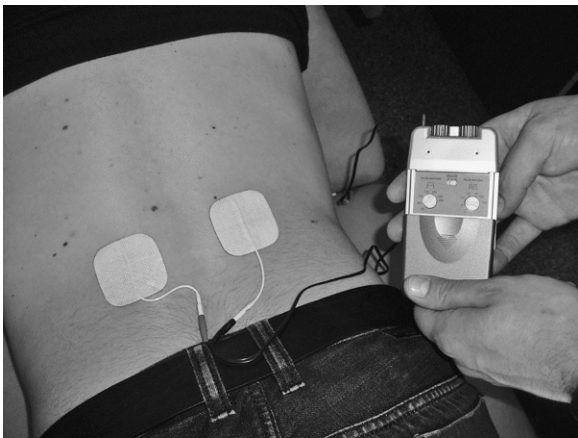
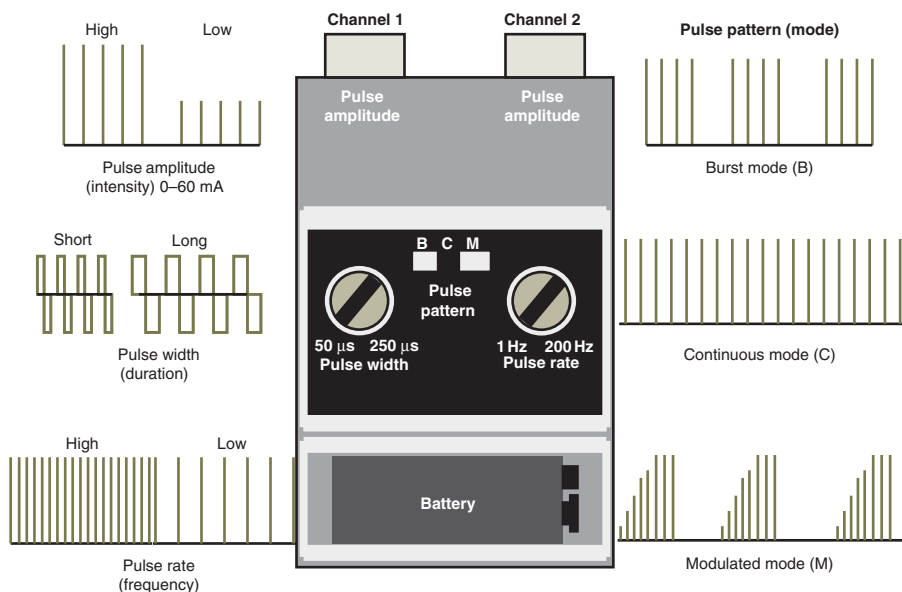


Figure 15.1 TENS administered on back using a standard TENS device.

## BOX 15.1

Transcutaneous electrical nerve stimulation (TENS) is the delivery of pulsed electrical currents across the intact surface of the skin to stimulate peripheral nerves, principally for pain relief.



**Figure 15.2** Output characteristics of a standard TENS device.

These ‘standard TENS devices’ usually deliver currents with pulse widths (durations) of 50–500  $\mu$ s, pulse rates (frequencies) of 1–250 pulses per second (pps) and a variety of pulse patterns (modes), including continuous (normal), burst (intermittent trains of pulses) and modulated amplitude, modulated frequency and modulated pulse duration (Fig. 15.2). Lead wires relay currents to reusable self-adhering knitted stainless steel electrode pads, commonly square electrodes 50×50 mm, which are attached to the skin surface. Standard TENS devices can be purchased without prescription from pharmacy stores or over the internet in many countries (Chipchase et al., 2009). TENS is used as a stand-alone treatment or in combination with pain medication for symptomatic relief of pain of any origin (Table 15.3; Fig. 15.3) and has been shown to reduce drug dosage, side effects and costs (Bjordan et al., 2003; Chabal et al., 1998). TENS has been used successfully for children as young as 4 years of age (Merkel et al., 1999). Various forms of TENS are also used to manage incontinence (Hagstroem et al., 2009), constipation (Clarke et al., 2009), the progression of dementia (Cameron et al., 2003), postoperative nausea and vomiting (Ezzo et al., 2006) and to facilitate wound and bone healing (Gardner et al., 1999). In general, evidence for success in these non-painful conditions is limited.

## TENS EQUIPMENT

TENS equipment consists essentially of (i) the stimulator (TENS device); (ii) the connecting lead wires; (iii) the electrodes (see Fig. 15.1). The manufacture of TENS equipment is a profitable exercise, and as a consequence new models are launched on the market frequently. This situation

**TABLE 15.3 ■ Examples of acute and chronic pain conditions that have been treated with TENS**

Speciality	System	Tissue	Acute	Chronic
Medical	Musculoskeletal	Muscles	Sprained or torn muscles, sports injuries	Myofascial pain, fibromyalgia
		Bones	Fractured rib	Rib with cancer deposit, osteoarthritis, rheumatoid arthritis
		Joints	Sprained or torn ligaments, arthritis, sports injuries	Osteoarthritis, rheumatoid arthritis
	Nervous system	Peripheral	Herpes zoster infection	Postherpetic neuralgia
			Acute vertebral collapse	Spinal nerve compression, causalgia
		Central	Acute stroke	Poststroke pain (thalamic pain), multiple sclerosis
	Cardiovascular	Cardiac muscle	Angina pectoris	Raynaud's disease venous graft scars
	Visceral	Pancreas	Acute pancreatitis	Chronic pancreatitis
		Liver	Acute hepatitis	Enlarged liver due to cancer
Surgical	Integumental	Skin	Trauma, surgical wound pain	Painful scar
Gynaecological	Reproductive	Uterine muscle	Dysmenorrhoea, labour pains	Pelvic pain, endometriosis
Dentistry	Dental	Teeth	Pulpal infection	Periodontal disease
		Orofacial	Acute orofacial pain	Temporo-mandibular joint

This list is representative and not exhaustive.

makes it bewildering for the would-be purchaser who is unfamiliar with TENS equipment. Before purchasing a particular instrument, the potential buyer should check that it incorporates some essential features (Table 15.4). Clinics may wish to stock a bank of different type of stimulators and electrodes, and it is well worth piloting different stimulators to determine how effective, reliable and economical they are from the point of view of patients and staff who will be using the equipment. Reusable self-adhering electrode pads made of knitted stainless steel are readily available and in various shapes and sizes. Recent developments include glove, sock and belt electrodes (Cowan et al., 2009).

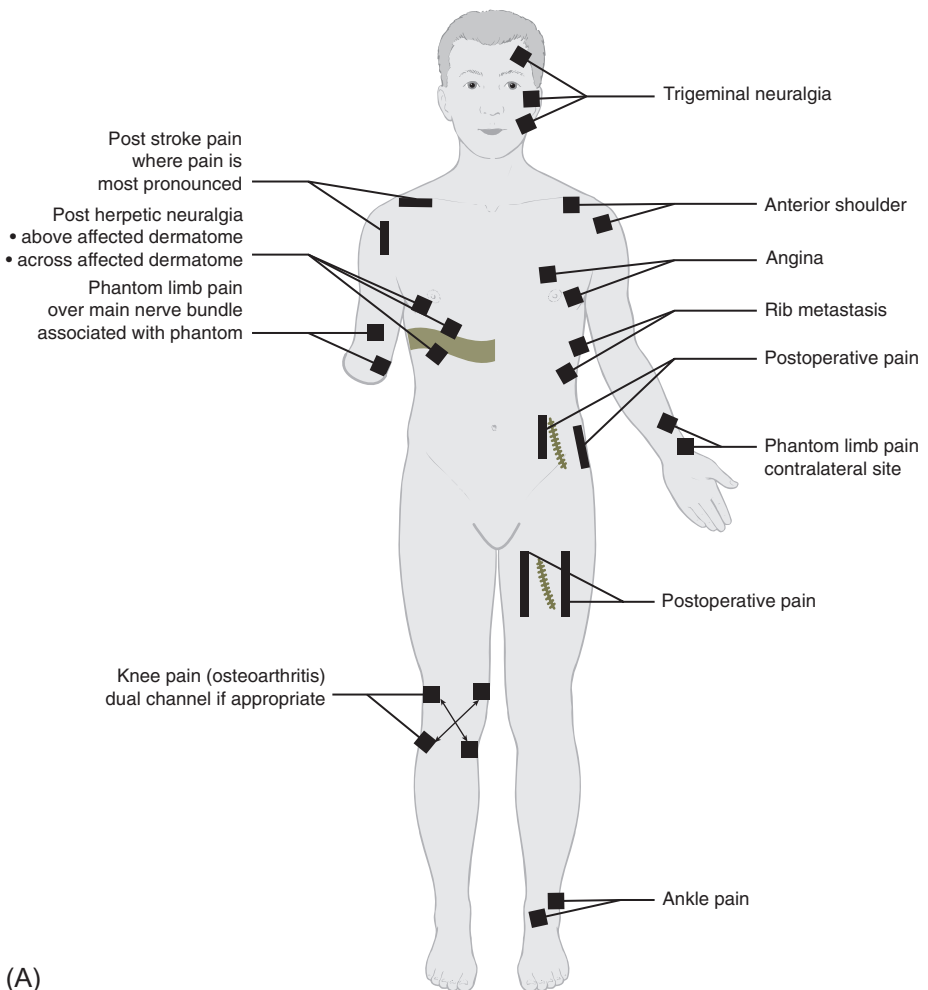
**TENS TECHNIQUES**

It is crucial that patients and staff understand that TENS therapy involves the use of appropriate technique. The main TENS techniques described by the International Association for the Study of Pain (Charlton, 2005, p. 94) are:

- conventional TENS (low intensity, high frequency) to stimulate low threshold non-noxious mechanosensitive afferents (A-beta fibres) arising from dermatomes related to the site of pain, without concurrently activating high threshold noxious afferents (A-delta and C fibres);

- acupuncture-like TENS (AL-TENS) (high intensity, low frequency) to stimulate high threshold mechanosensitive afferents (A-delta fibres) from cutaneous and deep (muscular) structures. AL-TENS is a form of ‘hyperstimulation’ and is administered to painful sites, acupuncture points, trigger points and over muscles. In clinical practice, large amplitude currents would be necessary to stimulate high threshold fibres in deeper structures such as skeletal muscle. However, using large amplitude currents would cause pain because the electric field would stimulate cutaneous nociceptive fibres in superficial structures. Therefore, AL-TENS is usually administered over low threshold motor efferents to generate phasic contractions in skeletal muscle which in turn causes activity in small-diameter skeletal muscle afferents.

In clinical practice, TENS is administered according to broad principles rather than specific prescriptions (Table 15.5). Conventional TENS is used in most instances with AL-TENS used for patients not responding to conventional TENS. Clinical experience suggests



(A)

**Figure 15.3** Electrode positions for painful conditions. (A) Anterior view

(Continued)

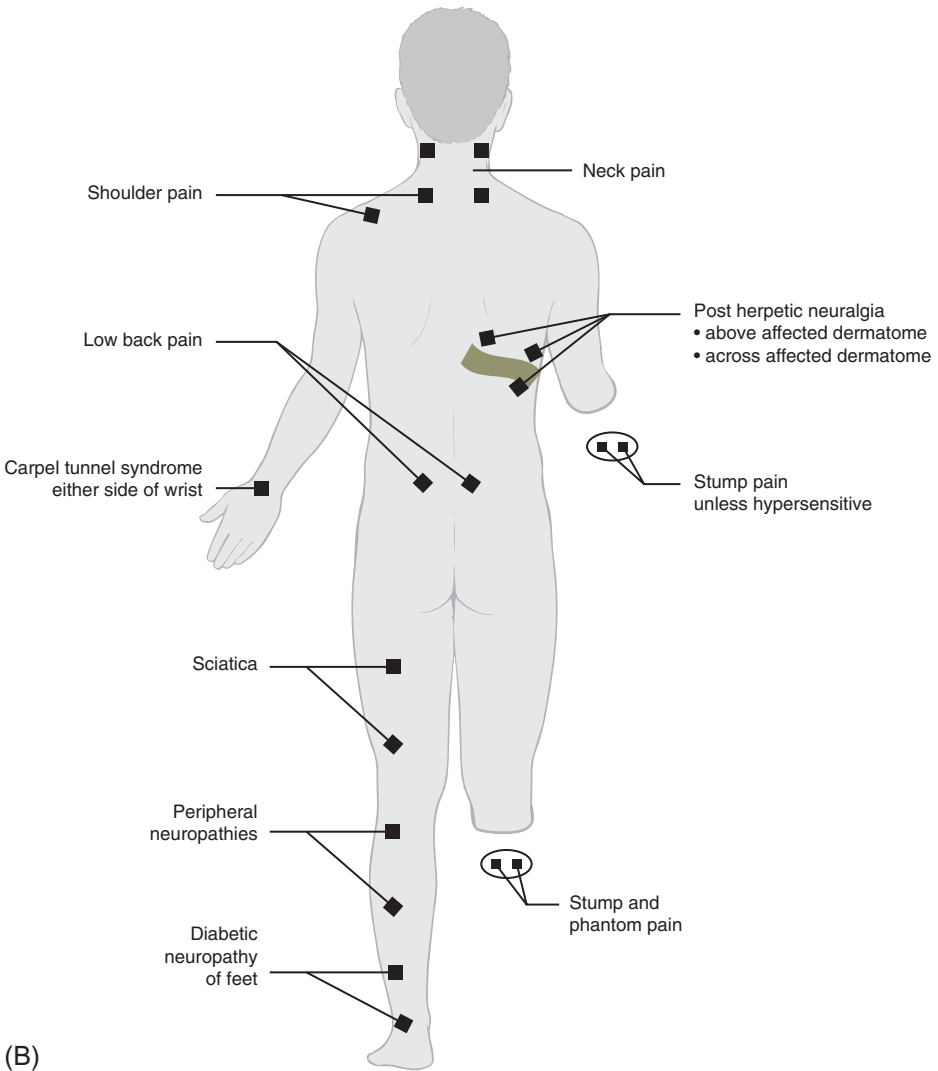


Figure 15.3, cont'd (B) Posterior view

that conventional TENS may be better for pains that are predominantly nociceptive, namely skeletal, paravertebral and joint pains and also visceral referred pain. AL-TENS may be found better for radiating neuropathic pain, especially where hyperaesthesia and/or dysaesthesia are prominent features and for pain arising from deep structures (Johnson, 1998; Sjölund et al., 1990; Johnson and Bjordal, 2011).

During conventional TENS patients are advised to increase current amplitude to achieve a strong, non-painful electrical paraesthesia within the painful region. A strong non-painful TENS sensation is indicative of selective activation of non-noxious afferents (A-beta) which has been shown to reduce transmission of pain-related information in the spinal cord and brainstem via segmental mechanisms (see section 'Mechanism of Action of TENS'; Fig. 15.4). Patients often use frequencies of between 10 and 200pps and continuous pulse patterns, although they are

**TABLE 15.4 ■ Technical specifications and essential features of a standard TENS device and its accessories**

Output specifications of device	Characteristics	Considerations
Pulse amplitude	Most devices deliver constant current output which is adjustable between 1 and 50 mA into a 1 k $\Omega$ load	On-off/amplitude (intensity) and frequency controls should be of convenient size and shape, easily adjustable yet adequately protected from accidental knocking or disturbance
Pulse frequency (adjustable)	Adjustable between 1 and 200 pps	Step-wise control is helpful
Pulse duration	Adjustable between 50 and 500 $\mu$ s	Step-wise control is helpful
Pulse pattern	Adjustable continuous, burst (random frequency, modulated amplitude, modulated frequency, modulated pulse duration)	Availability of pulse patterns: continuous (conventional) and pulsed (burst) patterns are mandatory. A modulation (ramped) pattern is highly desirable, and random pattern is an added advantage
Pulse waveform	Symmetrical or asymmetrical Biphasic or monophasic	This is usually fixed by the manufacturer
Channels	1 or 2	Useful for widespread pain or to treat more than one pain simultaneously
Preprogrammed settings	Often claimed to treat specific types of pain	May be useful for patients who prefer a limited choice of settings or have difficulty accepting how to adjust other settings. There is no strong evidence that certain preprogrammed settings are better for specific types of pain.
Timer		Useful when using TENS to assist sleep
<i>Additional features</i>		
Cost	£15–150	
Dimensions and weight	Small device = 6 $\times$ 5 $\times$ 2 cm; large device = 12 $\times$ 9 $\times$ 4 cm (50–250 g)	The stimulator should be compact, lightweight, conveniently shaped, comfortable to wear and to handle, sturdily built and easily attachable to belt or pocket. Larger devices may be useful for patients with challenged dexterity.
Batteries	PP3 (9V) or AA (2 $\times$ 1.5V = 3V)	Low battery drain: where necessary (i.e. for intensive use) it should be possible to use the stimulator with rechargeable batteries for which a compatible, compact mains operated battery charger can be obtained
Electrodes	Self-adhering	Most modern day electrodes are self-adhering. They will deteriorate over time so it is important to replace regularly. Shelf life can be prolonged by applying a film of water before and after use, storing within the accompanying plastic bag and on the plastic sheet and storing in the fridge.
	Shape and size	Commonly square electrodes 5 $\times$ 5 cm. However, smaller and larger electrodes are available. Shapes include circular (small ones ideal for acupuncture points) and butterfly (ideal where skin creases over joints).
	Glove, sock and belt electrodes	May be useful for painful hands, feet and back

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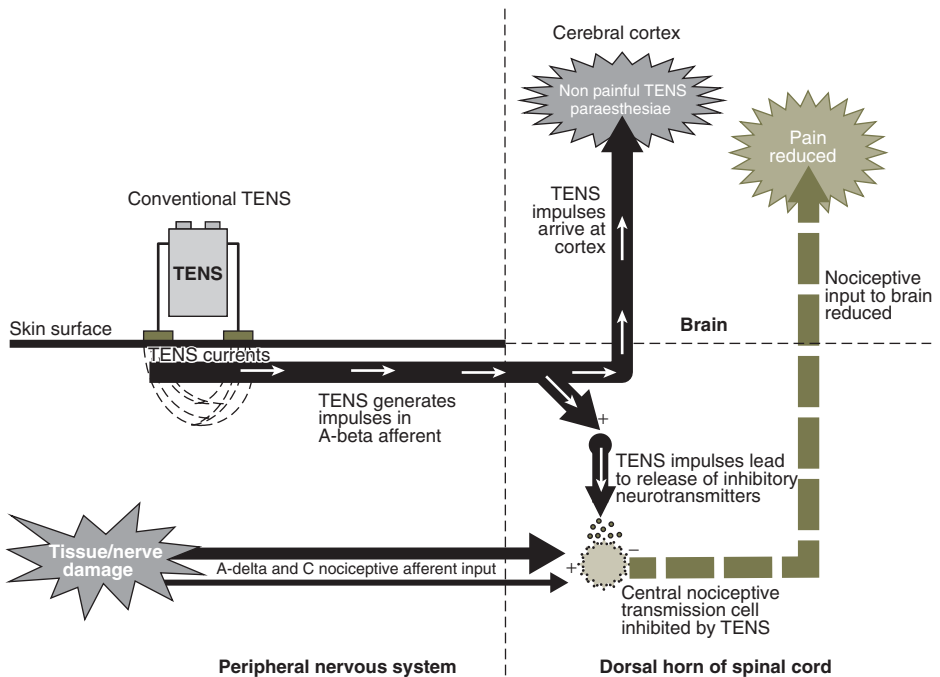
**TABLE 15.4 ■ Technical specifications and essential features of a standard TENS device and its accessories (continued)**

Output specifications of device	Characteristics	Considerations
Lead wires		The connecting lead(s) should be lightweight and flexible, comfortable to wear next to the skin and should connect to all standard types of electrodes
Support materials	Instruction manual with DVD Web support materials Helpline	A simple, lucid and well illustrated instruction manual is essential A helpline and maintenance and rapid replacement service operated postally or by courier service

**TABLE 15.5 ■ TENS techniques**

Characteristic	Conventional TENS	AL-TENS
Goal of stimulation	Activate cutaneous non-noxious peripheral afferents (A-beta)	Indirect activation of muscle afferents via TENS-induced muscle twitch
TENS sensation	Strong non-painful tingling TENS sensation (minimal muscle activity)	Strong non-painful pulsating TENS sensation with concurrent muscle twitching
Electrode positions	Dermatomal – straddle site of pain. Use main nerve bundle or contralateral positions in presence of hyper or hypo sensitive skin	Myotomal – over muscle belly or motor nerves at site of pain Use main nerve bundle or contralateral positions in presence of hyper or hypo sensitive skin Trigger points or acupuncture points sometimes used
Pulse amplitude (intensity)	Sufficient to achieve non-painful TENS sensation (low intensity)	Sufficient to achieve non-painful pulsating TENS sensation or muscle twitching (high intensity)
Pulse frequency (rate)	High (10–200pps) and determined by patient preference	Low (<5pps or <5 bursts (trains) per second of high frequency pulses)
Pulse width (duration)	Between 50 and 200 $\mu$ s and determined by patient preference	Between 100 and 200 $\mu$ s. Lower pulse width will generate a weaker TENS sensation yet still create muscle twitching
Pulse pattern (mode)	Continuous in first instance but subsequently determined by patient preference	Burst or amplitude modulated in first instance. If delivering low frequency single pulsed currents then use continuous
Dose	Use whenever pain relief is required. Can be used throughout the day although have a break every hour or so	Use for no more than 30 min at a time a few times each day as muscle fatigue may develop resulting in delayed onset muscle soreness the following day
Time course of pain relief	Rapid onset and offset of effects. Pain relief via segmental mechanisms (i.e. spinal gating)	Rapid onset delayed offset of effects. Pain relief via a combination of spinal gating and descending pain inhibitory pathways

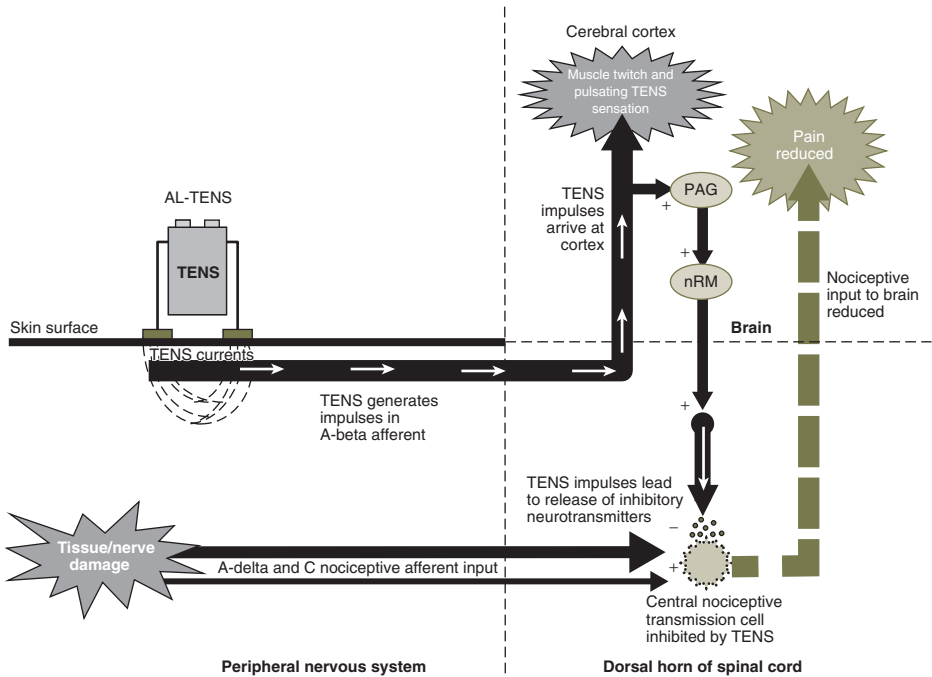
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**Figure 15.4** Simplified mechanism of action of conventional TENS. Activity in A-delta and C nociceptors excites (+) central nociceptive transmission cells in the spinal cord via neurotransmitters such as substance P (cutaneous nociceptors) or vasoactive intestinal peptide (VIP; visceral nociceptors). Central nociceptive transmission neurons project to the brain via spinothalamic and spinothalamic tracts to generate the perception of pain. Activity in A-beta afferents produced by conventional TENS leads to inhibition (–) of central nociceptive transmission neurons via the release of inhibitory neurotransmitters such as gamma-aminobutyric acid (GABA, black interneuron). Paraesthesia during conventional TENS is generated by information travelling to the brain via the dorsal columns.

encouraged to experiment with stimulator settings to maintain the most comfortable stimulation for that moment in time.

During AL-TENS higher intensity currents are used and delivered as low frequency single pulsed currents (e.g.  $\leq 5$  pps) or as low frequency bursts of high frequency pulses (e.g.  $\leq 5$  Hz bursts of 100 pps). Literature emphasises the need to use higher intensity currents during AL-TENS. Patients will not tolerate TENS at painful levels so most practitioners deliver AL-TENS at strong non-painful intensities that are often similar to that used for conventional TENS. However, if electrodes are positioned over muscles or motor nerves the low frequency currents used during AL-TENS will generate visible muscle twitching. Originally, AL-TENS was developed as a means to generate muscle twitching for pain relief, yet uncertainty still remains as to whether twitching is a prerequisite for an effect (Francis and Johnson, 2011; Johnson, 1998). AL-TENS using single pulses can be unpleasant producing painful muscle contractions, so trains of high frequency stimuli repeated at a low frequency (burst mode pattern of stimulation) are commonly used (Eriksson et al., 1979). Nowadays modulated patterns of stimulation are available including ramped amplitude in which each set of electrical pulses form a rising staircase of increasing intensity producing a stroking sensation which is more comfortable for the patient. AL-TENS has been shown to activate descending pain inhibitory pathways to reduce transmission of pain-related information in the spinal cord and brainstem (see section ‘Mechanism of Action of TENS’, Fig. 15.5).



**Figure 15.5** Simplified mechanism of action of AL-TENS. Activity in A-delta and C fibre nociceptors excites (+) central nociceptor transmission neurons which project to the brain contributing to pain perception. Activity in small-diameter muscle afferents (A-delta) during AL-TENS causes activation of brainstem structures such as the periaqueductal grey (PAG) and nucleus raphe magnus (nRM) which form the descending pain inhibitory pathways that excite (+) inhibitory interneurons ( $-$ ) in the substantia gelatinosa of the spinal cord. These inhibitory interneurons release met-enkephalin (black interneuron) which reduces activity in central nociceptive transmission cells (dotted line). Sensations associated with muscle twitching and pulsating AL-TENS are relayed to the brain via the dorsal columns.

Other suggested TENS techniques include ‘Acu-TENS’ which describes TENS on acupuncture points using a wide variety of parameters (Brown et al., 2009) and ‘Intense TENS’ which describes high frequency painful TENS given for short durations for wound-dressing changes, suture removal and venepuncture. Since the introduction of TENS, sustained efforts have been made to improve efficacy, and in recent years there has been a proliferation of TENS-like devices for pain relief (Table 15.6). Production of TENS-like devices has often been driven by developments in technology rather than proven efficacy or biological rationale, and therefore it is wise to try a standard TENS device in the first instance (Johnson, 2001, 2014).

## Treatment plan

### INDICATIONS FOR TENS

Essentially, TENS can be used to treat any localised pain of nociceptive, neuropathic or musculoskeletal origin. It is important to note that certain central pain states, for example, brachial plexus avulsion injury and that which follows injury of the spinal cord, may respond well to TENS but often require much experimentation in order to determine the optimum position of the electrodes. TENS can also be used in the treatment of pain of visceral origin such as angina pectoris and dysmenorrhoea. TENS is usually least effective for the treatment of pain which is

TABLE 15.6 ■ Characteristics of TENS-like devices

Device	Characteristics
Action potential simulation (APS) (Odendaal and Joubert, 1999)	Monophasic square pulse with exponential decay delivered by two electrodes. Pulse amplitude low (<25 mA), duration long (800 $\mu$ s–6.6 ms), frequency fixed at 150 pps
Codeatron (Herman et al., 1994)	Pulsed square wave delivered randomly to one of six electrodes. Pulse amplitude low, duration long (1 ms), frequency low (2 pps)
H-Wave stimulation (Blum et al., 2008)	'Unique' biphasic wave with exponential decay delivered by two electrodes. Pulse amplitude low (<10 mA), duration long (fixed at 16 ms), frequency low (2–60 pps)
Interferential therapy (interference currents) (Johnson and Tabasam, 2003; Palmer and Martin, 2008)	Two out of phase currents that interfere with each other to generate an amplitude modulated wave Traditionally, delivered by four electrodes; some devices have amplitude modulated waves that are premodulated within the device (two electrodes). Pulse amplitude low, amplitude modulated frequency 1–200 Hz (carrier wave frequencies ~2–4 kHz)
Microcurrent, including transcranial stimulation and 'acupens' (Koopman et al., 2009; Tan et al., 2006)	Modified square direct current with monophasic or biphasic pulses changing polarity at regular intervals (0.4 s) delivered by two electrodes. Pulse amplitude low (1–600 $\mu$ A with no paraesthesia), frequency depends on manufacturer (1–5000 pps). Many variants exist (e.g. transcranial stimulation for migraine and insomnia; acupens for pain)
Transcutaneous spinal electroanalgesia (TSE) (Palmer et al., 2009; Thompson et al., 2008)	Differentiated wave delivered by two electrodes positioned on spinal cord at T1 and T12 or straddling C3–C5. Pulse amplitude high, yet no paraesthetic sensation generated. Pulse duration very short (1.5–4 $\mu$ s, frequency high (600–10 000 pps)
Pain@Gone (Asbjorn, 2000; Ivanova-Stoilova and Howells, 2002)	Hand held pen device using piezoelectric elements to deliver a low ampere high voltage single monophasic spiked pulse (e.g. 6 $\mu$ A/15 000 V). Delivered by giving 30–40 individual shocks at the site of pain or on acupuncture points to generate non-noxious to mild noxious pinprick sensation – repeated whenever pain returns
Non-invasive interactive neurostimulation (InterX®) (Biggs et al., 2012; Gorodetskyi et al., 2007)	High amplitude, short pulse width, dynamic waveform delivered by closely spaced metal electrodes moved across the surface of the skin. Technology claimed to identify changes in tissue properties to identify optimal treatment locations
Limoge current (Limoge and Dixmieras-Iskandar, 2004; Limoge et al., 1999)	High frequency pulses interrupted with repetitive low frequency cycle delivered by three electrodes (negative electrode between eyebrows and two positive electrodes in retro-mastoid region). Used to potentiate effects of opiates
Salutaris TENS (Forst et al., 2004)	Dual channel stimulator delivering high (95 Hz) and low (4 Hz) frequency pulsed currents delivered by two electrodes using pulse widths of 100 or 280 $\mu$ s and current output up to 70 mA (into a 1 k $\Omega$ load). Uniqueness appears to be the use of a rising edge correction circuit 'to reduce the ramp time of each impulse and improve the therapy results'
MC5-A Calmare (Calmare® Pain Therapy Treatment) (Smith et al., 2010)	A large trolley based device that uses surface electrodes to simultaneously treat multiple pain areas using 'scrambler therapy'. Unable to find details of the output specifications of the device. Technology is claimed to substitute pain information with a synthetic non-pain information (Transcutaneous Electrical Modulation Pain Reprocessor)

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predominantly psychogenic in origin. The practical situation is that not every patient with the same type of pain will respond to TENS. Thus, the response to TENS is a function of the patient rather than the pain.

### Clinical points

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Key message: no pain should be considered untreatable by TENS until proved otherwise.

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## DIAGNOSIS BEFORE TENS THERAPY

As with all other forms of therapy, it is essential to diagnose the cause of the pain before attempting to treat it. However, when dealing with pain it is not always possible to make a precise diagnosis, particularly in the case of chronic pain. Therefore, what must be done is to ensure that the condition does not require some other form of urgent and/or more radical therapy, for example when contemplating the use of TENS to control pain caused by cancer. It cannot be emphasised too strongly that some pain conditions (including those of neoplastic origin) may demand a considerable amount of time and patience on the part of both patient and therapist to establish the most effective electrode positions. During this investigational phase it is also important to establish that TENS does not aggravate the pain condition; occasionally this occurs and when it does so usually indicates that this form of treatment is unsuitable for that patient.

## CONTRAINDICATIONS TO TENS THERAPY

There are safety guidelines for TENS in Australia, the UK and the USA and an excellent web-based resource at <http://www.electrotherapy.org>. Contraindications to TENS are relatively few (Table 15.7). Absolute contraindications include active implants such as pacemakers and ventricular assist devices, although sometimes medical specialists authorise use in certain circumstances. TENS produces inadvertent shocks with internal cardiac defibrillators (Holmgren et al., 2008) and artefacts on foetal monitoring equipment (Bundsen and Ericson, 1982). TENS can be used during pregnancy provided it is not administered close to the pregnant uterus (Coldron et al., 2007), and TENS can be used for patients with epilepsy provided it is not administered to the neck or head. There are reports of TENS inducing seizures in individuals susceptible to seizures due to co-existing psychomotor disturbances or following stroke (Rosted, 2001). TENS should not be delivered close to bleeding tissue or active epiphysis and should be used with caution for patients on an anticoagulant treatment (Houghton et al., 2010). TENS should not be delivered over local cancerous deposits, except in the palliative care setting (Johnson et al., 2008). Electrodes should never be placed over the anterior neck as this may generate a hypotensive response and syncope and also a laryngeal spasm. Moreover, electrodes should never be placed on the anterior and posterior chest to administer high intensity TENS because tetanic contraction of muscles over the thorax may compromise breathing (Mann, 1996). TENS should never be used while operating hazardous equipment, including motor vehicles.

## Complications

Serious complications from TENS appear to be very rare. In some individuals TENS may produce a vasovagal response leading to nausea, dizziness and even syncope, so it is very important to take time when using TENS on a patient for the first time. There are no known reports of electrical burns with TENS, but more commonly with TENS-like devices and then usually due to inappropriate technique (Ford et al., 2005; Satter, 2008). Contact dermatitis and minor skin irritation

TABLE 15.7 ■ Contraindications and precautions

Condition	Contraindication	Consideration
Active implants (e.g. pacemaker)	Contraindication	Applies particularly to on-demand pacemakers. Nevertheless, it is possible to operate fixed-rate pacemakers in the presence of a TENS machine, but this should never be done without the permission of the consulting cardiologist responsible for the patient and also, if necessary, the advice of the manufacturers of the pacemaker and the TENS equipment
Bleeding tissue	Contraindication	May increase blood flow
Patients with learning difficulties, who are non-compliant or who have a fear of, or rooted objection to, the use of electricity for medical treatment	Contraindication	The safety of the patient
Pregnancy	Local contraindication	Do not stimulate over a pregnant uterus. When TENS is being used for obstetric analgesia electrodes are applied posteriorly
Malignancy	Local contraindication	Do not stimulate close to 'treatable' local cancerous sites because may theoretically stimulate growth. In patients close to the end of life TENS can be used over malignant tissue if it provides relief of pain and other symptoms
Active epiphysis in children	Local contraindication	Do not stimulate over the active epiphysis because electrical currents may affect growth activity. If this were to occur it is likely that this would only be at high intensities rather than normal TENS intensities
Epilepsy	Local contraindication	Stimulation should be below the neck
Inflamed, infected or otherwise unhealthy skin	Local contraindication	Place electrodes on healthy skin proximal to area
Anterior part of the neck	Local contraindication	This is to avoid the possibility of stimulating the nerves of the carotid sinus or the larynx, which could produce hypotension or laryngeal spasm, respectively
Metal implants	Precaution	No known adverse effects with TENS although a skin burn has been reported for TENS-like devices

Many of the contraindications and precautions are theoretical and disputed, with limited evidence of consequence in clinical practice. These are the guidelines from one source, where they are discussed <http://www.electrotherapy.org/contraindications>.

is more common and often due to deteriorating electrodes or a reaction to the electrode. Irritation of the skin can be minimised by ensuring that the area to which the electrodes are to be applied is kept dry and free from grease and cosmetics. By this means the electrical resistance between the electrode and the skin is kept as low as possible and evenly distributed, thus avoiding 'hot spots' due to the presence of islands of low resistance through which electrical current flow is higher. It is important for all users and prescribers of TENS to be aware of this important and preventable problem.

TENS can be used over metal implants with care although there is one case report of a skin burn using interferential therapy, a TENS-like device, over a metal implant (Ford et al., 2005). Care must be taken if TENS is to be used with stents, percutaneous central catheters or drainage systems because muscle contractions inadvertently generated during TENS could create mechanical stress. Likewise, it is wise not to deliver TENS close to transdermal drug delivery systems because this may cause iontophoresis and so lead to drug toxicity.

Failure of TENS equipment due to faulty leads, stimulator, battery or charger, is uncommon. The lead wires remain the weakest link in the chain, with failure particularly at the end the leads where these are joined to the electrodes, usually via a pair of plugs and where fracture of the leads may occur. It also needs to be remembered that both disposable and rechargeable batteries have a finite life and that the latter cannot be recharged indefinitely.

### Safe technique and trial period

It is important to supervise the use of TENS by a patient for the first time to ensure to educate them on safe technique, expected therapeutic outcome and to assess whether it aggravates pain (Box 15.2). It is critical that the patient experiences the variety of TENS sensations achieved from the device and are aware that they should site electrodes on healthy skin with functional nerves and normal sensation. Practitioners can check that the skin is sensate using a simple 'blunt' and 'sharp' test where the patient closes their eyes and the practitioner presses as blunt (e.g. rear end of a pencil) and a sharp (e.g. cocktail stick) object against the skin and the patient identifies which is which. Comparisons are made with adjacent and contralateral areas. The patient needs to be assessed for competency for self-administration of TENS. It is best to advise patients to administer TENS in 30 min treatment sessions a few times a day when using TENS at home for the first time to ensure it does not cause an increased amount of pain due to increased activity permitted by TENS-related pain relief. However, patients should adjust usage to an 'as needed' basis after a few days, and they should experiment with stimulator settings between and within treatment sessions so that they achieve the most comfortable pulse frequency, pattern and duration. They should be told that electrodes can be left *in situ* and the device attached to a trouser or dress belt so TENS can be administered intermittently throughout the day.

Experience has shown that the best way to find out whether or not TENS will produce effective pain relief is to loan the patient a stimulator for a trial period of, say 1 month, so that it can be given an exhaustive test under normal everyday conditions of the patient's life. During the month's trial period, the patient is encouraged to contact the clinic in order to report progress. Initially, each patient on TENS therapy should be reviewed at monthly intervals and thereafter according to need.

### POST-TENS ANALGESIA

When analgesia induced by TENS persists after the stimulator has been switched off, poststimulation analgesia is said to occur. Only about 50% of patients are fortunate enough to experience this phenomenon. In those in whom it does occur, the duration varies from less than 30 min to over 2 h and obviously confers a number of advantages. First, it is an added convenience to the

TABLE 15.8 ■ The main systematic reviews and meta-analyses of TENS for pain relief

References	Condition	Data set and analysis	Reviewers' conclusion	Comment
<i>Acute pain</i>				
Walsh et al. (2009) Cochrane review	Acute pain	12 RCTs (919 patients) Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes
Carroll et al. (1996)	Postoperative pain	17 RCTs (786 patients) Descriptive analysis	Evidence of no effect	Comparison groups consisted of active and inactive interventions. Patients allowed free access to analgesic medication in some RCTs
Bjordal et al. (2003)	Postoperative analgesic consumption	21 RCTs (964 patients) Meta-analysis	Evidence of effect	Demonstrated that adequate TENS technique critical for effect
Freyenet and Falcoz (2010)	Post-thoracotomy pain	9 RCTs (645 patients)  Descriptive analysis	Evidence of no effect as stand-alone treatment Evidence of effect as adjuvant	Most studies low quality with small sample sizes
Carroll et al. (1997)	Labour pain	10 RCTs (877 patients) Descriptive analysis	Evidence of no effect	Comparison groups consisted of active and inactive interventions. Patients allowed free access to analgesic medication in some RCTs
Dowswell et al. (2009) Cochrane review	Labour pain	19 RCTs (1671 patients) Descriptive analysis	Evidence inconclusive	Low quality studies
Proctor et al. (2003) Cochrane review	Primary dysmenorrhoea	7 RCTs (213 patients) Descriptive analysis	Evidence of effect – pain relief for HF TENS only	Low quality studies with small sample sizes
<i>Chronic pain</i>				
Nnoaham and Kumbang (2008) Cochrane review	Chronic pain	25 RCTs (1281) Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes and possibility of under dosing TENS
Johnson and Martinson (2007)	Musculoskeletal pain	32 RCTs on TENS, 6 RCTs on PENS (1227 patients) Meta-analysis	Evidence of effect	Criticised for using multiple diseases creating heterogeneity

Continued on following page

TABLE 15.8 ■ The main systematic reviews and meta-analyses of TENS for pain relief (continued)

References	Condition	Data set and analysis	Reviewers' conclusion	Comment
Khadiolkar et al. (2008) Cochrane review	Low back pain	3 RCTs (197 patients) Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes and possibility of under dosing TENS
Poitras and Brosseau (2008)	Low back pain	6 RCTs (375 patients) Descriptive analysis	Evidence of effect	Low quality studies with small sample sizes
Dubinsky and Miyasaki (2010) Expert panel report	Low back pain	2 RCTs (201 patients) Descriptive analysis	Evidence of no effect	Small sample sizes and possibility of under dosing TENS
Rutjes et al. (2009) Cochrane review	Knee osteoarthritis	18 RCTs (275 patients) Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes with some RCTs not using standard TENS device
Bjordal et al. (2007)	Knee osteoarthritis	7 RCTs (414 patients) Meta analysis	TENS effective in short term	Accounted for adequate TENS technique in analysis
Brosseau et al. (2003) Cochrane review	Rheumatoid arthritis	3 RCT (78 patients) Meta-analysis	Evidence of effect	Low quality studies with small sample sizes
Robb et al. (2008) Cochrane review	Cancer pain	2 RCTs (64 participants) Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes and possibility of under dosing TENS
Kroeling et al. (2009) Cochrane review	Neck disorders (whiplash associated disorders and mechanical neck disorders)	7 RCTs on TENS (88 patients) Descriptive analysis	Evidence of effect but low quality studies	Low quality studies with small sample sizes and possibility of under dosing TENS. Included any surface electrical stimulation (ES) including microcurrent devices
Bronfort et al. (2004) Cochrane review	Chronic headache	3 RCTs Descriptive analysis	Evidence inconclusive	Low quality studies with small sample sizes and possibility of under dosing TENS

*Neuropathic pain*

Price and Pandyan (2000) Cochrane review	Poststroke shoulder pain	4 RCTs (170 patients) of any type of surface electrical stimulation	Evidence inconclusive	Low quality studies with small sample sizes and possibility of under dosing TENS. 2 RCTs used TENS to produce muscle contractions
Crucchi et al. (2007) Task force report	Various neuropathies	9 controlled clinical trials (200 patients) Descriptive analysis	Evidence of effect	Low quality studies with small sample sizes
Mulvey et al. (2010) Cochrane review	Postamputation pain	0 RCTs	No evidence available	
Jin et al. (2010)	Painful diabetic neuropathy	3 RCTs (78 patients) Meta analysis	Evidence of effect	Low quality studies with small sample sizes. Used non-standard TENS devices
Dubinsky and Miyasaki (2010) Expert panel report	Painful diabetic neuropathy	3 RCTs (2 RCTs used in evaluation 55 patients) Descriptive analysis	Evidence of effect	Low quality studies with small sample sizes

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**BOX 15.2 ■ Safe technique when using TENS on a patient for the first time**

- Check contraindications and precautions
- Determine appropriate site for electrodes and test skin for normal sensation
- Set TENS parameters when device is switched off as follows:
  - Pulse pattern (mode) = continuous (normal)
  - Pulse frequency (rate) = mid range (~60–80 pps)
  - Pulse duration (width) = mid range (~100–200  $\mu$ s)
  - Timer (if available) = continuous
- Connect electrode lead wires to electrodes
- Position electrodes on skin at site of pain or over main nerve bundle
- Connect electrode lead wires to TENS device
- Switch TENS device on but keep current amplitude at zero. Ask patient whether they feel a sensation from TENS – they should not
- Slowly increase intensity until patient reports the **very first TENS ‘tingling’ sensation**
- **Hold at this intensity for a minute** and ask patient whether the sensation is acceptable. If patient finds this very low intensity of TENS unpleasant then cease treatment; or if the patient agrees proceed with caution as the patient may experience an unwanted effect, for example, a vasovagal response
- Slowly increase the intensity of TENS until patient reports a strong but non-painful TENS sensation. Ask whether the sensation is acceptable and monitor patient for any signs of an autonomic response
- Encourage patient to experiment with settings by:
  - reducing amplitude so TENS barely perceptible
  - change the setting
  - therapist should suggest a phrase to describe what strength of stimulation is expected, for example, ‘strong but comfortable’
  - increase pulse amplitude to a strong non-painful level.

patient because it reduces the time needed for electrical stimulation and consequently reduces battery consumption. It also enables the patient to plan their treatment in advance and so ensure that analgesia will be available at a particular time, for example, during an important social event. Second, it enables the patient to have intervals unencumbered with TENS apparatus, although modern equipment is very compact so this is not usually a problem. When a patient’s pain is found to respond to TENS, it is important to discover whether the bonus of post-TENS analgesia occurs so that full advantage can be taken of this effect.

## CHANGES IN PATIENT RESPONSE TO TENS

It is important to monitor regularly each and every pain and its response to treatment. When a patient with chronic pain responds favourably to a trial with TENS, it is not possible to know whether this response is likely to be maintained or is likely to wane. When the latter occurs, it may be due to changes in the intensity and/or quality of pain, for example due to the addition of a neuropathic (neurogenic) component to a primarily nociceptive pain. Sometimes one or more new pains have become added to the original pain or the emotional response of the patient to the pain may have changed. Alternatively, the initially favourable response may have been a placebo response or there may be a change in the response of the patient to TENS. Experience suggests the waning response may be due to the onset of tolerance to TENS, which usually develops more slowly and insidiously than a placebo response and may not take place for many weeks or months after the start of treatment. It appears to be a similar phenomenon to that of drug tolerance which may develop over the course of weeks (e.g. opioid tolerance) or over the course of months or even years (e.g. insulin tolerance). Mechanisms contributing to TENS tolerance include waning neurotransmitter release or down-regulation of receptors concerned with the pharmacology of

pain and interference caused by the production of increasing amounts of endogenous opioid antagonists, for example CCK-8 which is the octapeptide form of cholecystokinin. Studies using animal models of nociception have demonstrated that repeated use of TENS generates opioid tolerance (Chandran and Sluka, 2003) with cholecystokinin (DeSantana et al., 2010) and N-methyl-D-aspartate (NMDA) receptors (Hingne and Sluka, 2008) involved. A similar effect has been found in healthy humans exposed to experimental pain (Liebano et al., 2011). It is known that regular patterns of neuronal activity encourage nervous system habituation and that delivering TENS regularly using the same settings could generate monotonous neuronal activity (Pomeranz and Niznick, 1987). It is for this reason that stimulators have been constructed with modulated pulse output to discourage the establishment of regular patterns of neuronal activity. There is evidence that modulated patterns of pulse delivery may help to reduce habituation and tolerance (Chen and Johnson, 2009; Desantana et al., 2008b).

## Optimal TENS technique

The crucial factors that determine outcome for TENS are the location of the electrodes and pulse amplitude (intensity). There is strong evidence from studies using humans exposed to experimental pain and from long-term responders to TENS that a strong, non-painful TENS sensation within the site of pain produces maximal analgesia (Bjordal et al., 2003; Claydon and Chesterton, 2008; Claydon et al., 2011; Johnson et al., 1991b). This is readily achieved using conventional TENS. For patients who do not respond to conventional TENS, or whose response declines over time, AL-TENS within the site of pain or over peripheral nerves proximal to the pain should be tried. In essence the optimum form of TENS for each patient is determined by a systematic process of trial and error.

### Clinical points

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A strong, non-painful TENS sensation within the site of pain produces maximal analgesia.

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## POSITION OF ELECTRODES

Electrodes are usually positioned on healthy sensate skin close to the site of pain so that TENS sensation permeates the painful area (see Fig. 15.3). With careful positioning of electrodes it is possible to project TENS sensations into distal body parts, for example, into phantom limbs to relieve phantom limb pain. If there is diminished skin sensitivity from nerve damage (e.g. numbness following peripheral neuropathy), it is unlikely that the patient will experience TENS sensation so electrodes are positioned proximally or contralaterally in the same dermatome. In the presence of tactile allodynia or dysaesthesia placing electrodes on the allodynic skin and/or permeating TENS sensations in the allodynic area may aggravate the pain, although paradoxically, this is not always the case. Thus, in the first instance, electrodes should be positioned over nerves proximal to the areas of tactile allodynia and care taken if TENS sensation permeates the painful area. Contralateral electrode sites in the same segment can be used in these circumstances. Likewise, care should be taken in the presence of dysaesthesias.

A variety of electrodes are available on the market including self-adhering electrodes of various shapes and sizes and also glove, sock and belt electrodes. In clinical practice 50×50 mm electrodes are most commonly used. There is tentative evidence that smaller electrodes (8×8 mm) may be more comfortable for stimulating superficial nerves (at depths of 1 mm in the skin) and larger electrodes (41×41 mm) for stimulating deeper nerves (at depths of 11 mm) (Kuhn et al., 2010). Recently electrode arrays to spatially target stimulation more precisely have been developed and are being piloted with some success (Kolen et al., 2012; Kuhn et al., 2009).

## ELECTRICAL CHARACTERISTICS OF TENS

TENS equipment makes it possible to vary the amplitude, frequency, width (duration) and pattern of currents applied to the body via electrodes (see Fig. 15.2). Originally, Sjölund and Eriksson demonstrated that low frequency (1–5 Hz)/high intensity stimulation produced analgesia which was blocked by the opioid antagonist naloxone whereas high frequency (>15–150 Hz)/low intensity stimulation produced analgesia that was unaffected by naloxone (Sjölund and Eriksson, 1979). Recently, it has been shown that high doses of naloxone block the hypoalgesic effects of high frequency (15–150 Hz)/low intensity stimulation too, suggesting that both forms of stimulation involve opioid mechanisms (Leonard et al., 2010). Also, patients who regularly take opioid medication appear to be less susceptible to benefit from AL-TENS (Leonard et al., 2011). However, there are few good-quality clinical or experimental studies that have compared conventional TENS to AL-TENS head-to-head, and those that exist are difficult to interpret because of a lack of standardisation in the way that conventional and AL-TENS were administered. Francis and Johnson found that AL-TENS generated longer lasting poststimulation hyperalgesia in healthy humans exposed to experimental pain compared with conventional stimulation (Francis et al., 2011). This is consistent with clinical experience, although to date no correlation has been found between specific electrical characteristics of TENS and responses for different types of pain. Evidence from studies in which pain-free human participants were exposed to experimentally induced pain suggests that a combination of amplitude, frequency and pattern influence pain relief, although research findings are inconsistent and often difficult to interpret (Claydon et al., 2011).

### Intensity of TENS (current amplitude)

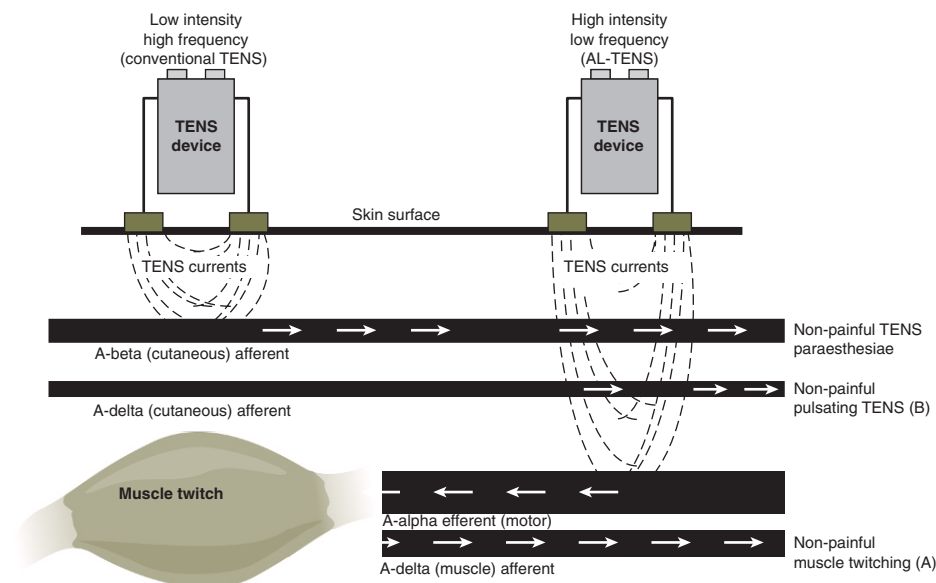
Long-term responders to conventional TENS titrate current amplitude to achieve a strong non-painful sensation, indicative of selective activation of low threshold afferent fibres (Johnson et al., 1991b; Fig. 15.6). Studies using healthy human volunteers demonstrate that strong non-painful high frequency TENS (i.e. conventional TENS) reduces non-injurious experimental pain more than a no current control and barely perceptible high frequency TENS (Aarskog et al., 2007; Lazarou et al., 2009; Moran et al., 2011). When using AL-TENS, current amplitude is increased and a strong, non-painful, pulsate-like sensation is experienced by the patient. This may generate muscle twitching depending on the strength of the current and where the electrodes are positioned. As the intensity of TENS sensation fades over time it is necessary to adjust pulse amplitude to maintain the strong non-painful TENS sensation (Pantaleao et al., 2011).

Delivering strong non-painful TENS punctuated with intense TENS may improve efficacy and is particularly useful for background pain with incidents of breakthrough pain (Sandkühler, 2000). Such an approach is taken when TENS is used during childbirth when the user presses a button on the obstetric TENS device to increase current amplitude and intensity to manage contraction pain.

The use of more channels (i.e. dual channel stimulation using four electrodes) will generate a stronger afferent input and stronger analgesia. Simultaneous stimulation at segmental and extra-segmental sites has been shown to generate stronger hypoalgesia compared with single channel stimulation (Claydon et al., 2008). Combinations of conventional TENS punctuated by periods of AL-TENS (i.e. sequential TENS) have been suggested as a means of improving efficacy (Sandkühler, 2000). Widespread chronic pains are perhaps less likely to respond to TENS although these problems can sometimes be overcome by the use of multiple electrodes connected to a multi-channel stimulator.

### Electrical pulse frequency of TENS

In recent years research has focussed on the role of pulse frequency when TENS intensity is standardised to generate a strong non-painful sensation. Evidence from non-human models of hyperalgesia has shown that the nervous systems response to TENS is frequency-dependent (DeSantana et al., 2008a; see section ‘Mechanism of Action of TENS’). Whether this translates



**Figure 15.6** Titrating TENS currents. Note that the low intensity currents excite mainly the A-beta (cutaneous) afferent fibres. By comparison, the high intensity currents stimulate (A) A-alpha efferent (motor) fibres and this produces non-painful muscle twitching that activates A-delta (muscle) afferents. High intensity currents might also stimulate (B) A-delta (cutaneous) afferents, although TENS amplitude should be reduced if this is painful. Activity in A-delta muscle and cutaneous afferents excite the descending PAG and nRM systems (shown in Fig. 15.5).

into meaningful differences in humans is less clear. A systematic review of experimental studies using healthy humans found that pulse frequency did not influence hypoalgesia during strong non-painful TENS, although most available studies were underpowered (Chen et al., 2008). Since then better quality studies have shown that strong non-painful TENS at 80 pps reduced experimental mechanical pain and ischemic pain when compared with 3 pps (Chen and Johnson, 2010b, 2011), but 3 pps was superior to 80 pps for cold-pressor pain (Chen and Johnson, 2010a). This suggests that the effects of frequency may depend on the modality of pain and that pains arising from different pathological states may respond differently to different frequencies of TENS. However, clinical studies have failed to detect a relationship between pulse frequency, type of pain and response to TENS (Claydon and Chesterton, 2008). Thus, most long-term users of TENS choose frequencies according to the comfort of the TENS sensation, and for that reason new patients are encouraged to select pulse frequencies according to what feels most comfortable for their pain (Johnson et al., 1991b; Oosterhof et al., 2008).

## Electrical pulse patterns of TENS

The pattern of pulses (mode) is chosen according to which TENS technique is being used (see Fig. 15.2). Continuous patterns (normal mode) is most commonly used for conventional TENS and trains of pulses (burst mode) chosen for AL-TENS. However, burst mode can be delivered at strong non-painful intensities without muscle contractions akin to conventional TENS and this has been described as pulsed mode TENS (Woolf and Thompson, 1994). Most long-term users of TENS prefer continuous patterns although up to one quarter may prefer burst mode (Johnson et al., 1991b). Experimental studies using healthy humans have failed to find differences in hypoalgesia for different pulse patterns during strong non-painful TENS when all other parameters were standardised (Chen and Johnson, 2009; Johnson et al., 1991a). Experiments using non-human models of pain have shown that modulated patterns of TENS delay the onset of tolerance to TENS effects (Desantana et al., 2008b).

## Waveform and pulse width of TENS

Most TENS devices use biphasic waveforms with zero net current flow between the electrodes to prevent electrolysis and skin irritation. Some devices use monophasic waveforms or biphasic waveform with an unbalanced net current. In these instances, the cathode activates the axonal membrane, so the cathode electrode (normally the black lead) is placed proximal to the anode. Manufacturers of TENS devices have attempted to modify current waveform in order to improve efficacy and comfort with limited success ([Hingne and Sluka, 2007](#)). At present, there is no strong evidence to support superiority of a certain waveform in standard TENS devices on the market, and most TENS manufacturers do not offer different waveforms within the device.

Commonly, pulse widths between 50 and 500  $\mu$ s are used. Reducing pulse width (duration) will facilitate currents through the skin so that deeper nerves and muscles can be stimulated without generating a particularly strong TENS sensation in the skin. In practice, when using conventional TENS pulse width (duration), pulse pattern and the position of red and black leads are determined by trial and error.

## OPTIMAL DOSAGE

Long-term responders administer TENS for many hours each day with pain relief being rapid in onset and offset with maximal benefit during stimulation, whilst the user is experiencing a strong non-painful TENS sensation ([Johnson et al., 1991b](#)). For this reason, patients are encouraged to use TENS throughout the day as needed. Over 50% of chronic pain patients who try TENS achieve benefit, but this appears to decline over time in some but not all patients ([Johnson et al., 1992](#); [Koke et al., 2004](#); [Sjölund et al., 1990](#)). Non-human studies have shown that repeated use of TENS encourages tolerance to TENS (see section '[Mechanism of Action of TENS](#)'), although a likely reason that some patients stop using TENS is that they feel that the effort needed to apply TENS regularly is disproportionate to the amount of pain relief obtained ([Koke et al., 2004](#)).

## Research on clinical effectiveness

There is much debate about the effectiveness of TENS for acute and chronic pain. A simple PubMed search using the MeSH 'transcutaneous electric nerve stimulation' reveals over 1000 hits for clinical trials, over 700 hits for randomised controlled clinical trials (RCTs) and over 30 hits for meta-analyses (7 Jul. 2011). A summary of systematic review findings is shown in [Table 15.8](#).

## ACUTE PAIN

By definition, acute pain is of short duration and therefore self-limiting. Pain that follows minor trauma is usually short-lived, and since it often responds to simple analgesics such as non-steroidal anti-inflammatories (NSAIDs) or paracetamol, TENS is not required. On the other hand, in sports clinics it is common practice to use TENS to treat localised pains which are the result of strains or tears of ligaments or muscles. Where multiple traumata are involved, it is not practical to use TENS, but instead an appropriate analgesic should be prescribed.

Historically, postoperative pain was the first form of acute pain for which TENS was used ([Hymes et al., 1974](#)), and the use of TENS to control labour pain was first reported by [Augustinsson et al. \(1977\)](#). Cochrane reviews have found evidence for TENS effectiveness for dysmenorrhoea ([Proctor et al., 2003](#)) but were unable to determine effectiveness for acute pain

(Walsh et al., 2009) and labour pain (Dowswell et al., 2009). National Institute for Health and Care Excellence (NICE) recommends that TENS should not be offered to women in established labour, although it may be beneficial in the early stages of labour (National Institute for Health and Clinical Excellence, 2007). In 1996, evidence suggested that TENS was not effective for postoperative pain (Carroll et al., 1997), although a subsequent meta-analysis of 21 RCTs (1350 patients) provided evidence of larger reductions in analgesic consumption when adequate TENS technique was used (Bjordal et al., 2003). In 2010, a systematic review provided evidence that TENS as an adjuvant relieved acute post-thoracotomy pain of moderate intensity and increased tolerance to coughing and pulmonary ventilatory function when used as an adjuvant to analgesics (Freynet and Falcoz, 2010).

### Clinical points

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Evidence shows TENS is effective for dysmenorrhoea, for post-thoracotomy pain and for postoperative analgesic consumption provided the technique is adequate.

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## CHRONIC PAIN

To date, the largest meta-analysis of TENS for chronic pain included 32 RCTs on TENS and 6 studies on percutaneous electrical nerve stimulation (1227 patients) and found that both techniques reduced chronic musculoskeletal pain (Johnson and Martinson, 2007). However, despite having good statistical power, there was criticism of heterogeneity due to combining multiple diseases (Novak and Nemeth, 2007). The most recent Cochrane review of TENS for chronic pain included 25 RCTs (1281 patients) with TENS superior to an inactive TENS control in 13 of 22 RCTs (Nnoaham and Kumbang, 2008). Variations in TENS technique and methodological quality prevented meta-analysis. A Cochrane review on osteoarthritic knee pain was inconclusive on evidence from 18 RCTs (813 patients) of which 11 RCTs used a standard TENS device (Rutjes et al., 2009) although an earlier meta-analysis (7 RCTs) found that TENS reduced pain by 22.2 mm (95% CI: 18.1–26.3) on a 100-mm VAS in the short-term when TENS was administered at optimal doses (Bjordal et al., 2007). Whether the magnitude of this reduction in pain is clinically meaningful has been a matter of debate (Dworkin et al., 2010). A Cochrane review of TENS for rheumatoid arthritis of the hand (3 RCTs, 78 patients) was inconclusive (Brosseau et al., 2003). NICE recommends that TENS should be used as an adjunct to core treatment for short-term relief of osteoarthritic knee pain (National Institute for Health and Clinical Excellence, 2008) and for rheumatoid arthritis of the hand (National Institute for Health and Clinical Excellence, 2009a).

### Clinical points

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Evidence shows an effect of TENS on musculoskeletal pain overall and for knee pain, though evidence is inadequate for other individual chronic pain conditions.

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The most recent Cochrane review of TENS for chronic low back pain was inconclusive (3 RCTs) with only 110 patients receiving TENS and 87 receiving placebo TENS (Khadilkar et al., 2008). The North American Spine Society recommended that TENS has immediate short-term effects to reduce pain intensity but not in the long-term, which was based on 6 RCTs with 375 participants receiving TENS and 192 receiving placebo TENS (Poitras and Brosseau, 2008). A meta-analysis of several therapies for non-specific chronic low back pain found that the effect

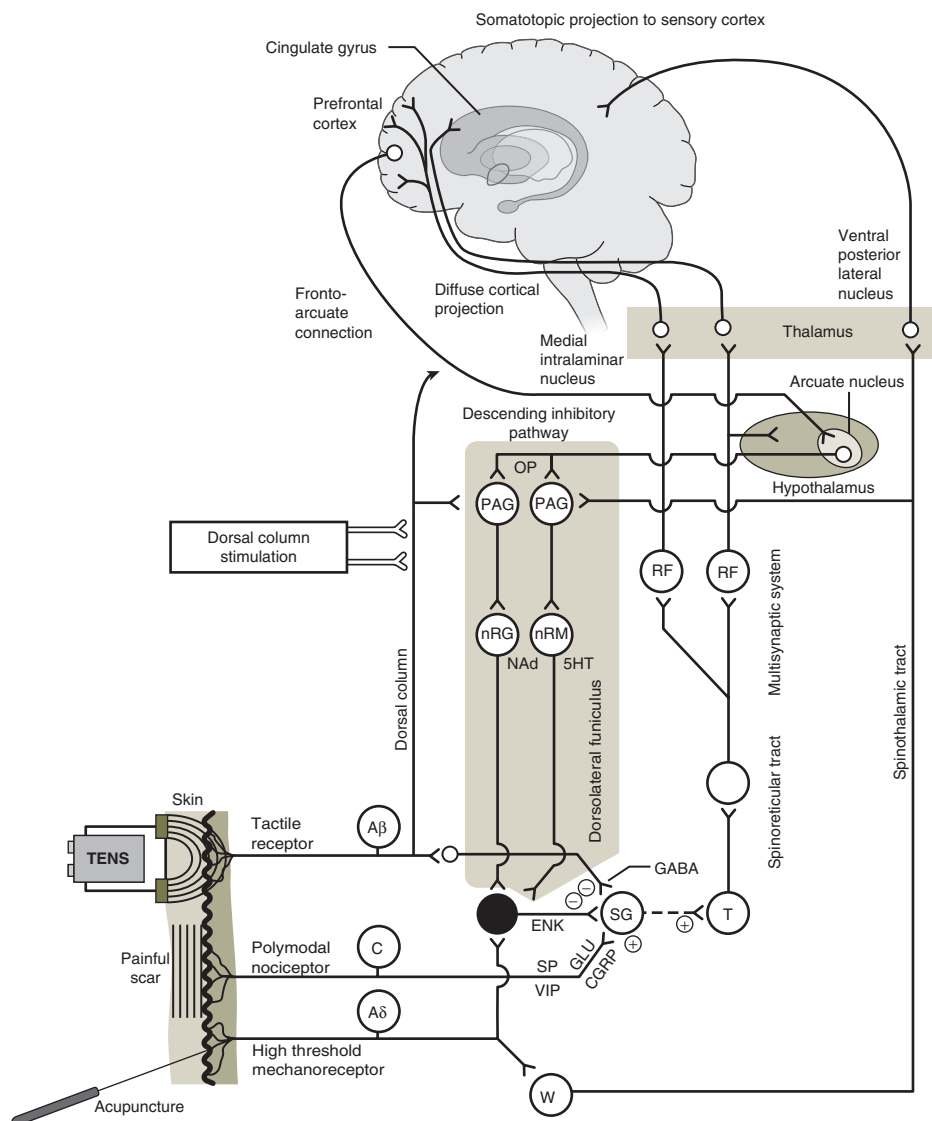
size for pain relief for TENS was small but similar in magnitude to NSAIDs and muscle relaxants (Machado et al., 2009). In 2010, the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology recommended that TENS should not be used for the relief of chronic low back pain (Dubinsky and Miyasaki, 2010). The reviewers claimed that their recommendation was based on good-quality RCTs, yet there were only 114 patients receiving TENS and 87 receiving placebo in the data set. NICE recommends that TENS should not be offered for early management of persistent non-specific low back pain (National Institute for Health and Clinical Excellence, 2009b). This was based on 3 RCTs conducted by two investigating teams, with 331 participants receiving TENS and 168 receiving placebo TENS.

There is a continuous flow of new RCTs on TENS yet uncertainty over the effectiveness of TENS for acute and chronic pain continues. A review of 38 RCTs from Cochrane systematic reviews on TENS for acute, chronic and cancer pain found that inadequate TENS technique and infrequent treatments of insufficient duration lead to negative outcomes and underestimation of TENS effects due to under dosing (Bennett et al., 2011). Other methodological shortcomings in RCTs of TENS include a failure to measure TENS effects during stimulation and a failure to monitor concurrent medication. It is not possible to truly blind TENS because the presence of a strong non-painful TENS sensation is a prerequisite of success although this bias can be reduced by the use of transient sham TENS devices that deliver currents to produce a TENS sensation for a short period of time before fading away to zero current output (Rakel et al., 2010). There is a need for universally accepted practice guidelines for TENS to reduce variability in clinical trial delivery and *ad hoc* clinical practice leading to a negative impact on patient care.

## Mechanism of action of TENS

On the basis of a considerable body of evidence it appears that both peripheral and central neuroanatomical and neuropharmacological mechanisms are involved in reducing pain during TENS (Fig. 15.7). In general terms, conventional TENS excites A-beta afferents connected to tactile receptors. After entering the spinal cord, these afferents ultimately ascend in the dorsal columns. At spinal cord level these A-beta afferent fibres give rise to collaterals which synapse with short interneurons which end close to the terminations of the C fibres as the latter synapse with substantia gelatinosa cells. These interneurons probably release gamma-amino butyric acid (GABA), which causes presynaptic blockade of the C-afferents, thereby preventing them from exciting the substantia gelatinosa cells and so blocking the onward transmission of nociceptive information.

At higher intensities TENS excites high threshold sensory receptors connected to small myelinated primary afferents (A-delta). One central branch of the A-delta afferent excites the inhibitory enkephalinergic interneurone (on the borders of the laminae I and II), releasing enkephalin which produces postsynaptic block of the substantia gelatinosa cell. This prevents the onward transmission of noxiously generated information. This mechanism explains the phenomenon of segmental effects of TENS and acupuncture. In addition, nociceptive-specific Waldeyer cells in lamina I of the spinal grey matter are excited via another central branch of A-delta primary afferents. The axons of the Waldeyer cells constitute another component (spinothalamic tract) of the crossed anterolateral funiculus and convey pinprick information to consciousness through the ventral posterolateral nucleus of the thalamus and thence to the somatosensory cortex (where there is somatotopic representation). Collaterals excite the PAG, which in its turn projects to the nucleus raphe magnus (nRM) situated in the midline of the lower brainstem reticular formation. Serotonergic (5HT) and noradrenergic axons of nRM cells descend through the dorsolateral funiculus of the spinal cord to synapse eventually with the cells described earlier, and so block the onward transmission of noxiously generated information in the same way as does segmental acupuncture. However, this descending inhibitory pathway gives off these connections at all levels of the spinal cord, thereby explaining extra-segmental effects of TENS and acupuncture.



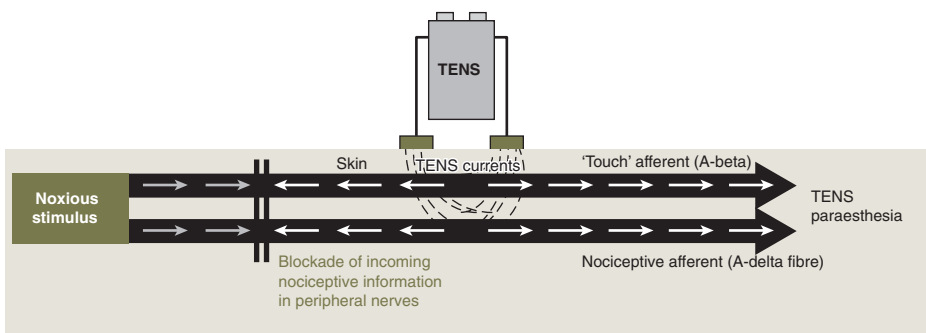
**Figure 15.7** More detailed anatomical diagram to show neuropharmacological circuits involved in acupuncture and TENS analgesia. The afferent pathways involved in transmitting nociceptive information from a painful scar to the higher centres via the dorsal horn, the ascending tracts and the thalamus are shown. The connections to the descending inhibitory pathways which descend in the dorsolateral funiculus are also shown. The connections to the hypothalamus are indicated. Abbreviations: Aβ, C and Aδ, represent the posterior root ganglion cells of Aβ, C and Aδ fibres, respectively; CGRP, calcitonin gene related peptide; ENK, enkephalinergic neuron; GABA, gamma-aminobutyric acid; GLU, glutamate; 5HT, 5-hydroxytryptamine, serotonin; NAd, noradrenaline, norepinephrine; nRG, nucleus reticularis; nRM, nucleus reticularis medialis; OP, opioid peptides; PAG, periaqueductal grey; RF, reticular formation; SG, cell in the substantia gelatinosa; SP, substance P; T, transmission cell; VIP, vasoactive intestinal polypeptide; W, Waldeyer cell; +, stimulant effect; −, inhibitory effect. (Reproduced with permission from Thompson and Filshie (1998).)

It seems likely that the amount of nociceptive information actually transmitted to the brain depends not simply upon the volume of the nociceptive signal but on the ratio of the nociceptive (noxious) signal to the non-nociceptive (non-noxious) signal. The amount of nociceptive information transmitted to the brain is also dependent on the relative contributions of descending pain inhibitory systems that reduce nociceptive transmission and descending pain facilitatory systems that enhance nociceptive transmission. Analgesia mediated by opioids results in part from interaction with these systems to enhance descending inhibition and reduce descending facilitation.

It is conceivable that extra-segmental acupuncture and AL-TENS may produce analgesia by activating the same opioid mechanisms. However, a striking and puzzling difference between analgesia produced by TENS and acupuncture is the duration of pain relief. Whereas TENS usually produces analgesia for minutes or hours, acupuncture can, and often does, produce analgesia for days or weeks (certainly after a course of acupuncture). The mechanisms discussed earlier cannot account for the prolonged analgesia commonly seen after acupuncture, so additional mechanisms (discussed elsewhere in this book) must be involved.

## RESEARCH EVIDENCE SUPPORTING THE MECHANISM OF ACTION

Electrophysiological studies on animal models provide strong evidence that TENS inhibits nociceptive-specific (e.g. Waldeyer) and wide dynamic range transmission cells in the spinal cord that respond to noxious stimuli (Garrison and Foreman, 1994, 1996, 1997; Leem et al., 1995; Ma and Sluka, 2001; Nardone and Schieppati, 1989; Sandkühler, 2000; Sandkuhler et al., 1997). Poststimulation effects last up to 1 h after TENS has been switched off and up to 2 h when TENS is given at intensities that recruit A-delta fibres (Sandkuhler et al., 1997; Sandkühler, 2000). TENS has been shown to activate descending pain inhibitory pathways including the ventrolateral PAG (Desantana et al., 2009). TENS also reduces nociceptive peripheral input to the central nervous system via a ‘busy-line’ effect on peripheral afferent information (Ignelzi et al., 1981; Nardone and Schieppati, 1989; Walsh et al., 1998) (Fig. 15.8) and at higher intensities will generate axon reflexes resulting in changes in activity in blood vessels, sweat glands and mast cells which may contribute to tissue-healing effects associated with TENS (Burssens et al., 2003, 2005). Autonomic efferent activity will also be modified during TENS resulting in increased peripheral blood flow and sweat responses (Sommer et al., 2011), although studies examining



**Figure 15.8** Peripheral mechanism by which TENS blocks incoming impulses in both touch afferent (A-beta) and nociceptive afferent (A-delta) fibres by a ‘busy-line’ effect. Thus, the more peripheral TENS electrode excites nerve fibres to conduct impulses in a peripheral (efferent, antidromic) direction that collide with nociceptive impulses that are moving in the opposite (afferent, usual) direction. On collision, the two sets of impulses extinguish each other and so reduce nociceptive and touch input.

the effects of TENS on the sympathetic nervous system are conflicting in their findings (Olyaei et al., 2004; Reeves et al., 2004). Brain imaging studies have shown that TENS modulates activity in primary and secondary somatosensory regions, primary motor cortex, supplementary motor cortex and the parahippocampal gyrus (Kara et al., 2010; Murakami et al., 2010).

### **Nociceptive pain**

Studies using models of joint inflammation in rodents have provided specific detail about TENS action. TENS at motor threshold increased tail flick latencies to noxious stimuli demonstrating that TENS reduces primary and secondary hyperalgesia (King et al., 2005; Radhakrishnan and Sluka, 2005; Sluka and Walsh, 2003; Sluka et al., 2006; Vance et al., 2007). High frequency TENS just below motor threshold reduced central sensitisation in rats when applied close to an inflamed area (Ma and Sluka, 2001) and also when TENS was applied to contralateral uninjured body sites (Ainsworth et al., 2006; Sabino et al., 2008). Activity in large diameter peripheral afferents from deep somatic tissues, but not cutaneous tissues mediated antihyperalgesia during TENS administered just below motor threshold (Radhakrishnan and Sluka, 2005). Hyperalgesia associated with low frequency TENS involved serotonin, noradrenaline and mu-opioid receptors whereas antihyperalgesia mediated by high frequency TENS involved GABA, noradrenaline and delta-opioid receptors in the central nervous system (Kalra et al., 2001; Sluka et al., 1999, 2006). When applied repeatedly in arthritic rats, TENS generated opioid tolerance (Chandran and Sluka, 2003), with cholecystokinin receptors involved (DeSantana et al., 2010).

### **Neuropathic pain**

TENS will interact with many of the physiological processes that contribute to sensory abnormalities experienced by patients with neuropathic pain including sustained amplification of sensory input via peripheral and central sensitisation, ectopic impulse generation due to expression of ion channels (Na<sup>+</sup>), neurotransmitters and receptors, and re-organisation of neural connections (Baron et al., 2010). Studies using chronic constriction injuries to peripheral nerves have shown that TENS reduces the responses of sensitised central transmission neurons to mechanical and thermal stimuli when applied to the receptive field and when applied contralaterally (Hanai, 2000; Leem et al., 1995; Nam et al., 2001; Somers and Clemente, 2003, 2006, 2009). These findings suggested that early intervention with TENS may reduce allodynia in humans with neuropathic pain (Johnson and Bjordal, 2011). The multiple site of action of TENS means that it is likely to affect pain transmission and experience for a range of different types of pain.

### **Concluding comments**

TENS devices have been used in mainstream medicine to relieve pain since the early 1970s. TENS is relatively inexpensive, safe and readily accessible. Published research supports its clinical usefulness and there is high quality evidence from electrophysiological studies demonstrating that TENS inhibits activity in nociceptive pain-related neurons in the peripheral and central nervous systems. In general, optimal TENS analgesia is achieved when the user experiences a strong non-painful TENS sensation close to the site of pain (i.e. conventional TENS). There has been a long standing debate about the efficacy of other electrical characteristics of TENS for different painful conditions. At present, TENS users are advised to use a systematic approach to determine the appropriate TENS settings. Systematic reviews and meta-analyses of RCTs on TENS effectiveness have been positive, negative and inconclusive and often include RCTs that deliver inadequate TENS technique and infrequent treatments of insufficient duration leading to under dosing and underestimation of TENS effects. Therefore, TENS should be considered as a treatment option although there is still a need for accepted practice guidelines to reduce *ad hoc* clinical practice.

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# Laser acupuncture

G.D. Baxter ■ S.M. McDonough

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## Introduction

*Laser acupuncture* describes a form of acupuncture treatment based upon the use of low power laser light to stimulate acupuncture points. The laser devices used in such treatments are usually diode-based 'pen' systems, which may be mains or battery powered, and are applied to the skin over the relevant acupuncture or trigger points to provide a noninvasive stimulation.

## History and background

Laser technology has found a variety of applications in medicine and surgery since the 1960s, initially in ophthalmology and surgery. Apart from the use of higher powered lasers which produce thermal reactions in tissues and are used clinically in surgery and for cancer treatments, lower powered nonthermal lasers have been researched and used since the 1970s to stimulate tissue repair mechanisms (so-called 'photobiomodulation', or low level laser therapy (LLLT)). The earliest research on this form of therapy was completed in Eastern Europe, China and Japan, initially using Helium–Neon (He–Ne) lasers, which were relatively low powered (1–2 mW) and cumbersome devices; it was not until the 1980s, with the introduction of higher powered and smaller diode-based devices, that this therapy first became more widely used in the West. In parallel with the development of LLLT treatments, initial reports appeared on the use of these laser devices to stimulate acupuncture points as a nonpenetrating alternative to needles.

Dr. Friedrich Plog is widely recognised as one of the pioneers within the field of laser acupuncture, first recommending the use of low power, nonthermal laser sources for the stimulation of acupuncture points for pain relief in 1973 (Whittaker, 2004). Plog's work also led to the commercial development of one of the first laser therapy systems designed specifically for acupuncture treatments (the *Akuplas*, designed and developed in Germany). However, it is important to note

that clinical use of low power lasers to stimulate acupuncture points had previously been reported in several centres, including Eastern Europe (Whittaker, 2004). In parallel with such developments in Europe, several groups in China, including Zhou and colleagues, also developed and trialled laser acupuncture systems for anaesthetic use in oro-maxillofacial surgery, with apparent success (Qin, 1987; Zhou, 1984). In assessing early developments in this field, it is also important to recognise that although Plog's work was the first to specifically focus on the irradiation of acupuncture points, it was not uncommon to see acupuncture points also being used as part of LLLT treatments particularly when treating painful conditions.

Early reports on laser acupuncture were typically anecdotal in nature or based upon small group, uncontrolled studies; the development of the field, at least in the West, was further delayed by the lack of English-language sources and resources on the topic. Controlled studies started to appear from the early 1980s, and the number – and quality – of such studies has increased steadily over intervening years (Baxter et al., 2008; Law et al., 2015).

The claimed benefits of laser acupuncture over other forms of acupuncture are primarily based upon its noninvasive nature being inherently safer and more acceptable for patients with needle phobia; treatment times are also relatively short, typically ranging 10s to less than a minute per point. In addition, in some cases laser acupuncture may require less training for the healthcare practitioner, and provide fewer regulatory hurdles, than is the case with needle acupuncture.

The development and use of laser acupuncture has not been without controversy, informed in part by the apparent lack of perceived stimulation during treatment and the associated lack of obvious mechanisms of action compared to needle or electroacupuncture (Robinson, 2014; Weissmann, 1979). Despite such apparent controversy, laser acupuncture has become increasingly popular as a form of acupuncture treatment, and the research foundation for the therapy has grown steadily, particularly over the last decade.

## Mechanisms of action

Unlike needle acupuncture, laser irradiation at the (nonthermal) parameters used for routine acupuncture treatment does not usually produce any sensation, and this represents perhaps the most controversial aspect of laser acupuncture treatment. (However, this does allow for better treatment concealment for the purposes of randomised controlled trials, as patients are more easily blinded to sham treatments.)

Mechanisms underlying the reported benefits of laser acupuncture are likely to be very different from those underlying needle acupuncture. Indeed, it is well recognised that therapeutic laser light has a range of biological effects, primarily related to tissue repair processes (Peplow et al., 2010, 2011). Such effects are collectively called photobiomodulation, and represent a parallel if not central element of the biological effects underpinning the observed clinical effects of laser acupuncture.

Perhaps more relevant, at least to the pain-relieving effects of laser acupuncture, is the wealth of studies, in humans as well as animals, focused on the peripheral neurophysiological effects of low power laser irradiation. A recent comprehensive review found consistent evidence of selective inhibitory effects of laser irradiation upon peripheral nerves, principally small diameter, thinly myelinated nerves (Chow et al., 2011).

## Clinical points

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Evidence shows laser acupuncture can have inhibitory effects on peripheral nerves.

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Investigation of the specific effects of laser acupuncture has included clinical studies which have incorporated detailed analysis to elucidate potential mechanisms of action, for example, in treatment of conditions such as hyperthyroidism (Ge et al., 1988).

Controlled laboratory studies, on humans and animals, have primarily investigated the central and peripheral neurophysiological effects of laser irradiation of particular acupuncture points (Hsieh et al., 2011; Litscher et al., 2010; Quah-Smith et al., 2010, 2013a,b; Read et al., 1996; Siedentopf et al., 2005) and also effects upon the cardiovascular system (He et al., 2012, 2013; Kostov and Bodurov, 1987; Litscher, 2010; Litscher et al., 2009, 2011, 2013; Wang et al., 2011). While findings are not totally consistent, most studies have reported changes in physiological measures such as evoked potentials and electrocardiographs as a result of laser irradiation of acupuncture points. However, it is important to stress that a number of the studies have been completed using custom or research laser systems which do not always reflect those in use in routine clinical practice, such as the use of needle guides, and a relatively high power violet laser system (wavelength 405 nm) by Litscher and colleagues, which produces *de qi* sensation during irradiation (Litscher, 2013). Therefore the degree to which reported effects in the laboratory represent potential mechanisms underlying the clinical effects seen with routine clinical laser acupuncture is unclear.

## Clinical application

### LASER DEVICES

For routine acupuncture treatments, laser devices are single source, diode-based systems which allow for easy application to specific points; alternatively fibre optic applicators may be used, through which laser light is delivered to the relevant point. Laser devices specifically designed for acupuncture treatments are widely available, as well as a (wider) range of therapeutic laser and light systems used for LLLT or photobiomodulation therapy, which provide options for laser acupuncture treatments.

Lasers produce light that is monochromatic (single coloured), is highly collimated (emitted rays of light are essentially parallel) and coherent (in time and in space). Laser devices are grouped into four classes (Table 16.1), depending upon the associated risk to the unprotected skin and unprotected eye, with class 4 lasers providing the greatest risk. Class 1 lasers are considered harmless and find wide applications in a range of devices such as disc players or as lecture theatre pointers. The lasers used in acupuncture treatments are generally Class 2 (low power) or 3B systems (medium power, the use of the 'B' in the label is historical and applies to old laser systems only), which are considered safe in routine clinical practice, subject to observation of simple safety measures, such as not applying the device near to the unprotected eye. Safety goggles should be used (by therapist and patient) when performing treatments, and any local or national regulations should be reviewed and applied; for example, in some cases, therapeutic laser systems may only be used in designated areas within a clinical facility.

TABLE 16.1 ■ Laser classes

Laser Class	Power	Thermal Effects
Class 1	Very low power, for example, CD players	Athermal
Class 2	Low power: emitting visible light 1 mW	Athermal
Class 3B	Medium power: emitting visible and invisible light <500 mW (0.5 W) significant ocular hazard	Athermal
Class 4	Above 500 mW significant hazard to skin and eyes also pose a fire risk	Thermal

For more information see MHRA guidance on laser classes ([http://www.dhsspsni.gov.uk/db2008\\_03\\_lasers.pdf](http://www.dhsspsni.gov.uk/db2008_03_lasers.pdf)).

## PARAMETERS

The key parameters which define laser treatments are as follows:

*Power* (generally specified in milliWatts or mW). The radiant power of the laser system used for treatment is a key factor in determining clinical effectiveness. Power output in commercially available systems varies widely, from 1 mW or less to several hundred milliWatts; however, the tendency in clinical and research applications has been to higher power outputs, with 10–100 mW outputs now considered the norm. Power output is usually fixed for a given laser system and is dependent upon the specification of the diode (or other lasing media) used in device manufacture. Direct-marketed lasers (i.e. advertised and sold to patients directly for self-treatment) are usually lower powered, battery-operated systems; quality assurance and provenance of some of these direct-marketed systems is also unclear. Power output should be specified on the laser device, and regular testing of the output is essential to ensure the safe and effective operation of the system as systems may not consistently produce the expected radiant power output (Nussbaum et al., 1999).

*Wavelength* (specified in nanometres or nm). Lasers produce a fixed wavelength monochromatic (single coloured) light with the emitted light clustered tightly around a single wavelength. This is in contrast to light produced by everyday light sources which appear white when viewed but emit across a range of wavelengths from the ultraviolet to the infrared. Wavelengths used in acupuncture laser treatments in clinical practice are usually in the visible red (e.g. 630 and 660 nm) or the infrared wavelengths (e.g. 830 and 880 nm). The wavelength of the laser is defined by its diode or lasing medium, and some systems allow use of different treatment probes or heads, providing the option of different treatment wavelengths. The clinical relevance of wavelength is due to wavelength-dependent absorption of light in biological tissues; the main result of this is that red wavelengths (>600 nm) are preferentially absorbed and therefore penetrate less than infrared wavelengths (approximately 700–1000 nm).

*Pulsing* (usually specified in hertz or Hz, i.e. pulses per second). Although most laser acupuncture systems in routine use are continuous wave, some advanced systems provide pulsing of the laser output, either as an option or as a fixed characteristic of the output. Pulsing frequencies range from several hertz to pulsing in the kilohertz range. While pulsing has been investigated in a number of controlled laboratory investigations, the clinical relevance of pulsing to effectiveness of laser acupuncture treatments is not clear (Law et al., 2015); however, a number of manufacturers claim specific frequency benefits for certain clinical conditions.

*Dosage* (usually specified as energy, in Joules per point, J per point). Dosage is typically calculated in J per point for laser acupuncture treatment and is a function of the power delivered by the device (in W) and time of application (in s):

$$\text{Dosage (J)} = \frac{\text{power (mW)} \times \text{time (s)}}{1000}$$

(Note: Joules is obtained by multiplying power in Watts, by irradiation time in seconds; thus, given that power for therapeutic devices is specified in milliWatts, the product of mW × s in the earlier formulas is divided by 1000.)

Using this formula, it can be calculated that a 30 mW laser device applied for a time of 30 s would deliver dosage of 0.9 J at the point treated, while a 1 mW system applied for 2 min (120 s) would deliver 0.12 J.

Alternatively, dosage may also be specified in energy density or radiant exposure (usually specified in J cm<sup>-2</sup>). This form of specifying dosage takes account of the total energy *and* the area of irradiation so that if the 0.9 J dosage specified earlier was delivered over a laser spot size of 0.1 cm<sup>2</sup>, the radiant exposure would be 9 J cm<sup>-2</sup>. This notwithstanding, for routine clinical practice, dosage specified in J per point is generally considered most appropriate.

Most modern devices will provide ‘dose’ as a user-selected option or allow a timed treatment to provide a prespecified dose. The clinical relevance of dosage is the same as for other forms of treatment: biological – and in turn clinical – effects are dosage dependent. While such dosage response is not definitively defined for all indications, it is clear from current evidence that clinical effectiveness of laser acupuncture for treatment of musculoskeletal pain and dysfunction depends on minimum doses of at least 0.5 J per point and use of power outputs of 10 mW or above (Baxter, 2009; Baxter et al., 2008).

### Clinical points

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For clinical effects, laser power output should be at least 10 mW and dose at least 0.5 J per point.

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## Application technique

Notwithstanding the inherent safety of laser acupuncture, the principles of good treatment practice apply: for example, patients should not be treated in the absence of a thorough history, examination and diagnosis, patient consent should be obtained, and adequate warnings provided concerning the risks and contraindications associated with laser acupuncture (see later).

The laser device to be applied during treatment should be approved for medical use and regularly tested for electrical safety and to check its output in keeping with relevant national and local regulations. In some jurisdictions operation of laser acupuncture devices is subject to those same safety regulations as for medical and surgical lasers (including designation of a laser safety officer, mandatory training for operators, limited safety key access and use of designated areas and warning signs).

Most modern devices will feature a mains-powered base unit, featuring a control panel, a safety key to prohibit unauthorised operation, and at least one treatment probe with a laser diode mounted in the tip. The control panel may be used for selecting the dose (or the treatment time as a proxy for dose) and pulsing frequency if this is provided as an option. With these parameters selected, the laser treatment probe is applied ‘in contact’ to the skin at the selected point and activated using the integral switch or trigger on the device. The probe should be applied to the skin with pressure, thus providing additional stimulation to the point; indeed, some have even recommended vigorous stimulation including ‘pecking’ of the laser probe into the tissue (e.g. ‘woodpecker’ technique as described by Ohshiro and Calderhead (1988)).

The treatment probe should be held in place to deliver the desired dosage/time before relocating the probe to the next point. Scanning or moving the head across the skin surface is not recommended for laser acupuncture treatments as this will reduce the effectiveness of the treatment and deliver less than the calculated or expected dosage per point (or area).

## Contraindications and precautions

As a nonpenetrating form of acupuncture point stimulation, low power laser devices may be considered safe for routine practice when simple contraindications and precautions are observed.

*Risk to the unprotected eye.* The greatest potential risk from the use of laser devices in acupuncture treatment is injury to the unprotected eye. As indicated earlier, protective goggles should be worn by the therapist and patient at all times during treatment given the Class rating of devices in routine clinical use. Direct intra-beam viewing should be avoided, and the patient warned of the attendant risk.

*Active or suspected carcinoma.* Given the potential of laser irradiation to stimulate tissue repair and other biological processes (i.e. through photobiomodulation), possibly at a distance from the site of application, treatment of patients with active or suspected carcinoma is regarded as a contraindication.

*Treatments in Pregnancy.* Stimulation of certain specific points was traditionally avoided in pregnancy (as for needle acupuncture), but as discussed in [Chapter 33](#) there is no evidence of harm arising provided the usual precautions are observed. Irradiation at sites directly over the pregnant uterus is recognised as an almost universal contraindication for all electrophysical agents in the first 3 months of pregnancy. Although effects on the foetus are not plausible, distress will be inevitable if abnormalities are later discovered.

These represent the primary contraindications to laser treatment, although it should be stressed that the risk of adverse event is limited; to date there have been no reports of significant adverse events specifically attributable to laser acupuncture treatment.

## Indications for treatment

The cardinal indication for laser acupuncture is pain relief: this was the original application for the therapy, in contrast to LLLT, which developed from laboratory-based work and clinical studies on tissue repair. This notwithstanding, benefits have been claimed for laser acupuncture – like other forms of acupuncture – in the management of a wide range of conditions including childhood asthma, chronic respiratory disease, postoperative nausea and vomiting, nocturnal enuresis, as well as pain of various aetiologies including chronic neck pain, headaches, back pain, arthritis and myofascial pain.

## MYOFASCIAL PAIN/TRIGGER POINTS

Treatment of myofascial pain and trigger points represents the primary application for laser acupuncture. Evidence from two systematic reviews consistently shows moderate evidence of benefit, at least where adequate treatment dosage is applied (at least 0.5J per point) ([Baxter et al., 2008](#); [Law et al., 2015](#)).

### Clinical points

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Moderate evidence supports the use of adequate dose of laser acupuncture for myofascial pain.

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## OSTEOARTHRITIS

Studies of effectiveness of laser acupuncture in the management of osteoarthritis have produced mixed results ([Shen et al., 2009](#); [Yurtkuran et al., 2007](#)) while a recent well-publicised high quality trial by Hinman and colleagues reported only marginal benefits in knee osteoarthritis (less than the minimally important difference) ([Hinman et al., 2014](#)). This trial has however been criticised for using an inappropriately low dosage (0.2J per point). In contrast, other randomised controlled trials found benefits of laser acupuncture ([Al Rashoud et al., 2014](#); [Shen et al., 2009](#); [Yurtkuran et al., 2007](#)).

## LOW BACK PAIN

Despite apparently widespread use of laser acupuncture for the management of low back pain (acute, subacute and chronic), there is currently limited evidence of clinical effectiveness from randomised controlled trials performed in Australia and in Europe ([Glazov et al., 2009, 2014](#); [Ruth et al., 2010](#)). In contrast, a small study combining laser acupuncture with cupping found some benefits in terms of pain relief ([Lin et al., 2012](#)). As with treatment of osteoarthritis, some of these studies can be criticised for use of inappropriately low dosages.

## NOCTURNAL ENURESIS

Studies of laser acupuncture have shown mixed but generally positive results, particularly when combined with other treatments (Heller et al., 2004; Karaman et al., 2011; Moursy et al., 2014; Radmayr et al., 2001; Radvanska et al., 2011).

## SMOKING CESSATION

While an initial report indicated preliminary evidence of benefit for smoking cessation in adults, subsequent controlled studies have indicated no evidence of effectiveness in adolescents (Garrison et al., 2003; Yiming et al., 2000; Zalesskiy et al., 1983).

## OTHER CONDITIONS

Laser acupuncture has been recommended and benefits reported in controlled trials for a myriad of conditions including colitis and other gastrointestinal disorders (Zhang and You, 1987); some forms of sinusitis in children, particularly more chronic forms of sinusitis (Pothman and Yeh, 1982); radicular pain syndromes (Kreczi and Klingler, 1986; Sprague and Chang, 2011); chronic tension headache (Ebneshahidi et al., 2005) and headache in children (Gottschling et al., 2008) and temporomandibular joint pain (Hotta et al., 2010).

## Concluding comments

Laser acupuncture has become widely used as a form of acupuncture treatment, particularly in cases of needle phobia or where noninvasive stimulation is preferred over needles; laser acupuncture may also be an option for providing acupuncture treatments where regulatory barriers or training precludes use of needle acupuncture for some practitioners. Research on laser acupuncture has developed rapidly, focused on establishing the clinical effectiveness of such treatment in various conditions and on elucidating its underlying mechanisms of action. While there are moderate levels of evidence for laser acupuncture treatment of some conditions, particularly musculoskeletal pain, evidence for other applications is contradictory or lacking. Further high quality, controlled clinical research is needed in these areas to establish definitively the role of laser acupuncture in modern healthcare; as part of this, greater attention should be paid to basic biophysical principles of laser treatment and in particular the relevance of dosage.

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# SECTION 5

## *Research*

### SECTION OUTLINE

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# A critical approach to randomised controlled trials of acupuncture

M. Cummings ■ A. White

## CHAPTER OUTLINE

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## Introduction

This chapter aims to address the particular challenges of designing, performing and interpreting randomised controlled trials (RCTs) of acupuncture.

A clinical trial is “A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioural outcomes” (NIH website, accessed November 2015). In an RCT participants are allocated to one or other group by randomisation in order to try to balance groups for prognostic factors. An RCT may arrange that both participants and care providers are blinded to their group, for reasons discussed later. Such trials are called double-blind and provide the gold standard for evaluating new interventions (Cartwright, 2007; Meldrum, 2000).

The schematic [Figure 17.1](#) shows that any benefit of treatment may be due to the combination of specific effects of needling, and ‘non-specific’ effects of the overall acupuncture consultation process, as well as the process of being within a trial (Hawthorne effect) and some statistical factors (regression to the mean). More information about the effects is given in [Box 17.1](#). As discussed in detail later, there is no truly inactive ‘placebo’ acupuncture. All attempts at placebo actually provide acupuncture that is merely less active than ‘real’ acupuncture, and it is convenient and customary to call these attempts ‘sham’ acupuncture, not placebo.

Unfortunately, there are a number of factors other than the treatment itself that can have an effect on the symptoms or other measurements. They reduce the ‘truthfulness’ of the result. These factors can affect every aspect of the trial – the design, performance, analysis and reporting of the trial – and are discussed in detail later.

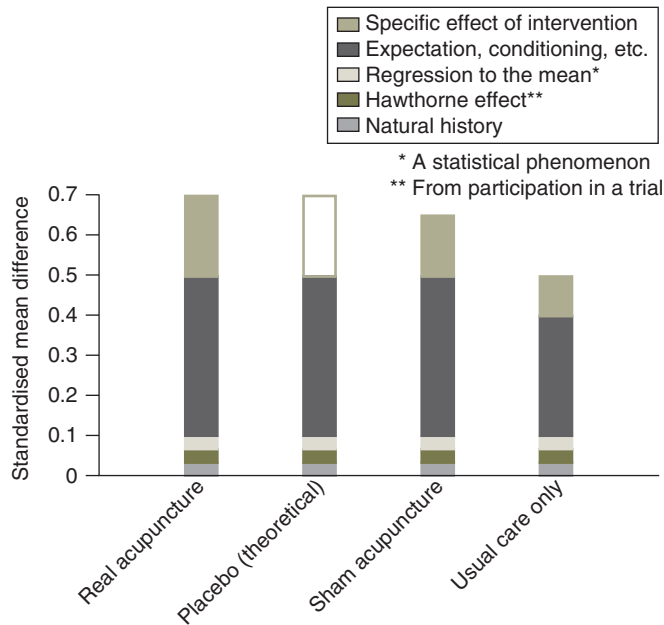


Figure 17.1 Clinical trial theory.

BOX 17.1 ■ Effects – specific and non-specific

**Specific effects of the intervention**

These are the effects that are solely attributable to the active intervention, excluding any psychological effects. Specific effects can be assessed only in a placebo-controlled trial by comparison to an inactive control. In an explanatory study of acupuncture the specific effect would be that of the needle stimulus.

**Non-specific effects of the intervention**

These effects are present in both active and placebo control groups in a placebo-controlled trial. They can be estimated in three arm trials by comparison of the placebo (or sham) control group with an observed group that receives no active or sham intervention.

**Other non-specific effects**

These effects are present in all groups in any clinical trial.

Natural history – this is a change from baseline measures seen in all groups attributable to the natural course of a condition, disease or symptom being measured.

Regression to the mean – this is a statistical phenomenon related to population sampling and using measures that are imprecise. It is seen in individuals that are included in research trials because their symptom score exceeds a threshold value. The actual level of symptoms in some of these patients is below the threshold, but their score at the moment of testing appears higher because of measurement error. In subsequent measurements, their score is likely to ‘regress’ to their mean, but this reduction in score does not represent any benefit.

The Hawthorne effect – this is a phenomenon whereby patients appear to improve as a result of being observed. The effect was first discovered after studying factory workers in Chicago.

Finally, there are factors peculiar to acupuncture studies that may reduce the potential for measuring real effects: the use of active sham controls (rather than true placebos) and lack of certainty about the optimal active treatment to use (Vickers, 2002; White et al., 2001).

Science demands that all these factors in the study should be carefully identified, addressed and minimised, if possible, to give the trial maximum chance of producing a result. This is a major challenge, and this chapter discusses the most important of these factors, and the attempts that have been made (or should be made) to address them in acupuncture trials.

This chapter aims to help the reader understand features of an acupuncture study and therefore interpret the published report critically. After general principles of study design and bias have been described, this chapter will use the structure of a trial to show how these principles are applied, proceeding from theory to practice.

### Explanatory and pragmatic trials

The approach to an RCT can be ‘explanatory’, or ‘pragmatic’ or more usually some combination of the two (Thorpe et al., 2009); these terms correspond to ‘efficacy’ and ‘effectiveness’ respectively. The former pair of terms apply more to the overall approach, and the latter pair apply more to the features of the design.

An explanatory study aims to provide new information about the intervention and its mechanisms – the commonest example being whether the specific effect of needles is superior to placebo. Other examples could be whether four needles are more effective than two, or electroacupuncture (EA) superior to manual acupuncture (MA). In all these examples, all other variables have to be tightly controlled, to produce ideal conditions to test the single factor – viz an ‘efficacy’ study (Table 17.1). This efficacy design has become closely associated with placebo-controlled trials, and so the term ‘efficacy of acupuncture’ has sometimes become restricted to refer to the specific effect of acupuncture needles, compared with placebo. (In other circumstances and often in the mind of the general public, the term efficacy is still used more loosely to mean any kind of effectiveness.)

A pragmatic approach aims to determine whether the treatment, including all its non-specific effects, should be applied in practice. The corresponding ‘effectiveness’ design reflects everyday practice as far as possible (see Table 17.1). And ‘effectiveness’ of acupuncture is widely used to refer to its effectiveness in every day practice, used in making clinical decisions. This tells us about ‘effectiveness’ of the treatment overall, not efficacy of the needles alone.

In the development of new drugs or technology, explanatory studies tend to precede pragmatic studies. In the case of traditional medicines that have been practised for centuries, the reverse is often the case as they are already in use in the community, and appear to be effective. This is certainly the case for acupuncture, and data on effectiveness preceded data on efficacy, with the latter still being debated.

There is a debate to be had about what evidence is needed for acupuncture to be offered as part of publicly funded health care in those countries, e.g. in the West, where it is not part of the

TABLE 17.1 ■ Differences between efficacy and effectiveness trials of acupuncture

	Efficacy design	Effectiveness design
Patients	Highly selected, homogeneous, many exclusion criteria, likely to complete the study	Heterogeneous, few exclusion criteria, enrolled as they present
Intervention	Exactly defined, precisely performed	As used in practice
Control	Well defined and standardised; likely to be placebo, sham or another form of acupuncture	Likely to be ‘usual care’
Outcome	Few but precise measurements, possibly laboratory tests	Patient-orientated: symptoms and quality and life

cultural heritage. Some emphasise a particular ethical dimension, arguing that an intervention should not be offered until its efficacy is confirmed, i.e. it is established as superior to placebo. Others argue that patients should not be denied access to an intervention that has proved itself both (1) more effective than, and (2) at least as safe as, other available treatments for the condition. There is data now to show that acupuncture has a very good safety record (White, 2006; White et al., 2004; Witt et al., 2009), and that it is effective in a number of chronic pain conditions (Cummings, 2009a; White and Cummings, 2009; Witt et al., 2006), perhaps even superior to existing treatments in some cases (Corbett et al., 2013). It is argued that on this basis it is justifiable to use the technique. Moreover, for spinal pain, osteoarthritis and headache the highest quality evidence shows the specific effect of acupuncture is superior to sham (Vickers et al., 2012), although there is a lack of similar clarity over the evidence for some other conditions.

## Placebo and sham

The term placebo needs to be used with care in scientific writing (Cummings, 2003) since it may be used to refer to a number of different things or phenomena (Benedetti, 2014; Finnis et al., 2010; Grünbaum, 1986). The term sham is less problematic.

The word placebo derives from the Latin verb *placere* 'to please', and in Latin *placebo* means 'I shall please'. Its first documented use was in ecclesiastical tradition in early translations of the bible, where 'Placebo Domino' was used to mean 'I shall please the Lord' (Gensini et al., 2005). It became used in the medical literature in the latter half of the eighteenth century to refer to a remedy used more to please than to heal people.

It is most familiar in healthcare research as a placebo or inactive pill used in a double-blind trial of a drug. Patients are unaware whether they have real or placebo pill so are unlikely to give biased assessments, and clinicians are blinded so their behaviour towards the patients, and their assessment of their progress, are not influenced. Hence the double-blind trial has become the gold standard in interventional trials.

The placebo effect is sometimes defined as the effect observed in the placebo group of an RCT; if the term is used to refer to the overall change from baseline in the placebo group of a trial (this is the effect in the placebo group, rather than the placebo effect) then it includes other effects such as natural history, regression to the mean and the Hawthorne effect (see Fig. 17.1). If it is measured against a no treatment group in the same RCT (the more correct way) then it may be a function of psychological effects of taking a placebo pill, such as expectation, conditioning, motivational concordance (Hyland, 2011) and so on. Either way, the effects are driven from activity in the brain.

The placebo response is the benefit accruing from the patient's belief that a treatment has been given – whether it has or not. This has been studied extensively, and we now know that the response can be modified by all manner of factors related to the context of care (see Chapter 7). It is probably better to refer to 'context effects' than to the placebo response, since many of these aspects relate to good clinical care, and the term placebo has negative connotations, i.e. an ineffective treatment, and being 'all in the mind'.

Physical therapies and surgical treatments that are subjected to explanatory trials maximising internal validity require patients to be adequately blinded in the control group. In order to do this a sham procedure is often used. It is difficult to know to what extent these sham procedures actually have real effects, since they are unlikely to be used in practice. There is a detailed discussion of sham acupuncture below.

## Formulating a research question

Researchers who are developing clinical trials should repeatedly define for themselves the precise research question they are addressing, since from this flows every aspect of the study design (patients, intervention, control and outcomes – PICO).

The types of question that RCTs are particularly designed to address are about efficacy and effectiveness, in various forms. The term acupuncture potentially covers a wide range of different therapeutic interventions, so it is important for the researcher to define what exactly is meant by ‘acupuncture’ within the context of their research question (Cummings, 2003).

In the context of clinical trials of WMA, acupuncture could be defined as the insertion and manipulation of fine filiform needles, omitting any reference to ‘acupuncture points’. In the context of clinical trials, we could add ‘in order to stimulate relevant changes in the nervous (or other) system’. The emphasis is on the degree of stimulation, not the precise location where it is given (see Chapters 1, 7 and 8).

Most sham-controlled trials of acupuncture have generally compared acupuncture with controls where:

- needles were inserted at ‘wrong’ points
- needles were inserted at the ‘correct’ points, but superficially
- blunt devices were pressed on the skin at ‘correct’ points.

Such trials test the effect of needle insertion and the effect of a precise acupuncture ‘point’. They depend on the traditional approach that the acupuncture effect is only seen at acupuncture points. They are not designed to answer the basic WMA questions about the efficacy and effectiveness of nerve stimulation by needles. In discussing the principles of the research question, we shall not consider such traditional designs any further here, but restrict ourselves to the neurophysiological approach.

There are three basic research questions with some variations.

1. Does acupuncture needling have any (physiological) effect?

This is the basic question about the ‘specific’ effect of acupuncture needles, i.e. effect beyond placebo. This requires an explanatory approach, and the design is likely to be ‘efficacy’, meaning effect under perfect conditions. To create those conditions, careful control is needed over the type of patient, excluding patients with comorbidities that could affect the response; highly standardised performance of acupuncture; outcome measures chosen as reliable rather than convenient; and narrow measurements of one symptom rather than patient quality of life (QoL). Since an inactive placebo is impossible, the control will consist of sham acupuncture designed to be as inactive as possible, such as without stimulation and not in relevant segments. Such a trial lies at the opposite end of the spectrum to ‘pragmatic’, and it is said to maximise internal validity at the expense of external validity (see preceding text, Table 17.1 and Boxes 17.1 to 17.4).

### BOX 17.2 ■ Explanatory and pragmatic approaches

#### **Explanatory**

Explanatory trials test whether an intervention can have a beneficial effect in ideal conditions.

#### **Pragmatic**

Pragmatic trials measure effectiveness; they measure the degree of beneficial effect in real clinical practice.

### BOX 17.3 ■ Efficacy and effectiveness

#### **Efficacy**

The effect of a treatment in ideal conditions, often measured as the effect beyond a placebo control in an explanatory RCT.

#### **Effectiveness**

The effect of a treatment in every day conditions, often measured as the effect beyond a no treatment control, or the effect when added to usual care, in a pragmatic RCT.

## BOX 17.4 ■ Internal and external validity

### Internal validity

Internal validity refers to the ability of a study method and its performance to correctly answer a research question in an unbiased manner.

### External validity

External validity refers to the degree to which a research study addresses a relevant topic in a manner reflecting day-to-day clinical practice of medicine. This is related to the generalisability or applicability of the results of a study.

Some people dismiss acupuncture as no more than placebo (Madsen et al., 2009), and think the only type of studies that should ever be performed on acupuncture are ones that are sham-controlled. Others note that sham acupuncture is not an available option (practically and ethically) in practice, so comparing real and sham acupuncture provides little useful clinical information; they are more likely to pose question 2 (Macpherson, 2004). It should be noted here that some acupuncture techniques appear to be very similar in physiological terms to the most common sham acupuncture technique, that is superficial needling. It seems likely that most sham techniques have some physiological activity, and therefore cannot be considered inactive placebos (Linde et al., 2010a,b; Vickers, 2002; White et al., 2001; MacPherson et al., 2014).

#### 2. Is acupuncture useful in clinical practice?

This question is of interest to patients and their personal physicians. It reflects the ‘effectiveness’ of the treatment in everyday practice, and is likely to use a ‘pragmatic’ approach (as opposed to explanatory) and an effectiveness design. Such studies aim to measure the effectiveness of an intervention in a real world setting, by comparing it with a control group that does not receive the intervention, but is on a waiting list, or receives usual care or a comparative intervention (perhaps the standard care for the condition). Patients with comorbidities are likely to be eligible, acupuncturists are more likely to be able to modify the treatment formula to reflect practice, and outcomes are more patient-relevant and likely to be longer term. The emphasis throughout is on external validity, but attempting to retain as much internal validity as possible. The results of such trials allow us to estimate the broad value of acupuncture treatment overall, but do not give us any idea of the relative contribution of the needles, the techniques, the point combinations or the acupuncture context effects. A good example of these would be the Acupuncture in Routine Care (ARC) trials performed as part of the extensive German trial projects known as the *Modellvorhaben Akupunktur* (Cummings, 2009a).

#### 2b. Is acupuncture cost effective?

The usual way to address this question of cost-effectiveness is as a parallel part of a study addressing question 2 (Witt et al., 2006). The cost-effectiveness question is for informing decisions in healthcare provision.

However, in the absence of primary cost-effectiveness data, health economic modelling can be attempted. A guideline development group under the auspices of the National Institute for Health and Care Excellence in the UK (NICE) has performed health economic modelling on acupuncture for osteoarthritis. The modelling was performed under the assumption that the fairest way to assess the effectiveness of acupuncture in practice was to use the difference between acupuncture and control in a variety of RCTs, most of which used sham acupuncture as the control. The estimates of cost attributed to the gain in QoL (a quality adjusted life year or one QALY) related to acupuncture treatment were broad, varying from well within the threshold for purchasing interventions (data from a pragmatic study) to well outside (data from efficacy studies).

The premise of this modelling has been much debated (Latimer, 2009; White, 2009), and it seems that for acupuncture it may not provide a reliable method of assessing cost-effectiveness (Cummings, 2009b; Latimer et al., 2012). Fortunately there is now a reasonable number and

variety of primary health economic evaluations of acupuncture (Ratcliffe et al., 2006; Whitehurst et al., 2011; Witt et al., 2006), which will hopefully preclude the desire to attempt any further modelling by NICE or others.

### 3. Does acupuncture have similar effectiveness to other treatments?

In some circumstances it may be relevant to ask whether or not two treatments have an 'equivalent' effect. For example if group acupuncture is considerably cheaper than individual acupuncture for treating a painful condition, it is important to know that it is no less effective. This requires an 'equivalence' trial in which the effects of the two treatments are tested to see if there is no clinically relevant difference at the 95% confidence interval. Note that this is different from testing whether a difference is present, and generally requires a much larger sample size. The arguments are slightly complex, but readers need to be clear that saying acupuncture is 'not significantly different' to counselling (for example) is not the same as saying the two are 'equivalent'.

### 4. Is acupuncture safe?

This question is not well addressed by RCTs since adverse events (AEs) are so rare they can only be identified in large numbers of treatment sessions – although data in RCTs should of course be collected and reported. Useful data can be produced by combining studies (White, 2004), but there has been one very large survey of AEs performed as part of the *Modellvorhaben Akupunktur* (Cummings, 2009a; Witt et al., 2009).

## Finding an answer to the question

The researchers' next task is to plan the study to produce as accurate and as true a result as possible.

Three general types of problem are recognised that can lead to the 'wrong' result. Two of these, confounding and error, can reasonably easily be identified and avoided; but the third, bias, is multifactorial and complex, and the principle constraint in clinical research on acupuncture. Unfortunately, 'bias' is rather easily wheeled out as a criticism of positive studies of acupuncture. A good understanding of these various problems ensures they are minimised in any study, and taken account of in interpreting results.

## CONFOUNDING

The assumption of the RCT assumes that the final difference between the groups is all due to the type of treatment to which they were allocated. Unfortunately there may be other things that have contributed: for example, several patients may also take analgesic drugs or visit physiotherapists, at their own choice, particularly in a pragmatic trial. The answer may not be just to stop them – that could be unethical – but at least to be aware, to measure it, and allow for it in the analysis. In studies of surgical or obstetric analgesia the pain scores may not be significantly different between acupuncture and control groups, since it would be unethical to withhold available analgesia, and the comparison groups often use more alternative analgesic methods, for example nearly twice the rate of epidural analgesia in a study of EA for labour analgesia (Vixner et al., 2014).

## ERROR

Two types of 'error' are recognised that may affect the trustworthiness of the result. The first is the obvious one – mistakes made in collection of data (the latter is mostly a human activity therefore subject to error). The second is the error introduced by natural variation between individuals, referred to above as 'chance': for example, even a group of patients who would all categorise their pain as 'severe' would actually provide different visual analogue score (VAS) scores, through the well-known natural variability. This makes for a lot of 'noise' in the data that can blur the 'signal' (or effect) that we are looking for. This noise can be accounted for by the well-developed procedures of statistics. Statistics includes, for example, ensuring that there are enough participants to

overcome the variability (noise) and provide a reliable answer. But these have to be understood and followed: perhaps the most common error in published acupuncture RCTs is that the sample size is too small to be definitive. Sure, the data can be analysed, but the analysis is almost meaningless – and interestingly it is similarly meaningless whether it is positive or negative. The best such small trials can do is to provide information on how big the sample size needs to be for a definitive trial to answer the research question.

### Clinical points

A sample size of 50 per group is the minimum needed to have a 4/5 chance of correctly identifying an effect size of 0.5 (i.e. the lower end of a 'moderate' effect size).

A depressing aspect of acupuncture literature is the number of small studies published that are labelled as pilot studies, when in fact they were planned as definitive trials but either failed to recruit the required sample – or did not even calculate it beforehand. The latter refers to a *power calculation*, and this tells you the number of subjects required to show the expected difference (estimated from prior research) in statistical terms, at a predetermined probability level and with some estimate of the variability (SD – standard deviation) of the relevant outcome measure in the population sample.

True pilot studies are crucially important in their own right in establishing the best way to organise a definitive study: but by definition they are not themselves designed to show differences between groups, so should not include a statistical analysis.

Error can also occur in analysing cross-over studies, since the size of the effect could be different whether a patient has treatment or control first (order effect); and the effect of the first intervention could influence the measurements second time round (carry-over effect).

## BIAS

In an RCT, bias results in an underestimate or overestimate of a treatment's true effect, resulting from some 'systematic' difference between the groups, other than the treatment itself (Box 17.5). Bias is a systematic error, or deviation from the truth, in results or inferences (Higgins and Green, 2011). The RCT is a research method used to test clinical interventions, which attempts to minimise bias.

### BOX 17.5 ■ Bias in clinical trials

#### Selection bias

Selection bias refers to systematic difference between characteristics of patients allocated to an active intervention or to a control group.

#### Performance bias

Performance bias refers to systematic differences in the care that is provided to groups other than the intervention being assessed.

#### Detection bias

Detection bias refers to systematic differences between groups in how outcomes are determined.

#### Attrition bias

Attrition bias refers to systematic differences between groups in withdrawals from a study.

#### Reporting bias

Reporting bias refers to systematic differences between reported and unreported findings.

#### Other bias

Relevant only in certain circumstances: for example carry-over in cross-over trials; recruitment bias in cluster-randomised trials; and contamination, whereby the experimental and control interventions get 'mixed'.

## Selection bias

Selection bias refers to systematic difference between characteristics of patients allocated to an active intervention or to a control group. In clinical practice we may choose patients for our favoured intervention that are more likely to improve, and we may refer on the more difficult cases. This would give us an inflated impression of the success of the intervention when applied to the entire population. The RCT attempts to minimise this form of bias by randomly allocating patients to active or control groups. When assessing the internal validity of a trial the precise method of randomly allocating patients (sequence generation) and the success of allocation concealment is considered. Allocation concealment means that the group to which each patient will be allocated by the randomisation process is concealed from the researcher when making the decision to enrol the patient in the trial.

## Performance bias

Performance bias refers to systematic differences in the care that is provided to groups other than the intended intervention being assessed. Blinding of (patients and) study personnel helps to ensure that patients in different groups are treated similarly. It is rare for acupuncture practitioners to be blind during the application of acupuncture, and although it is possible with one device, there are significant limitations to the acupuncture technique tested. Therefore most acupuncture studies are open to the accusation that the practitioner has, consciously or unconsciously, influenced the acupuncture group in a positive way, and/or the control group in a negative way. It is unclear whether practitioners can actually have such influence on patients yet still maintain blinding of those patients. Nevertheless, it remains a theoretical bias that has to be accounted for in interpreting results. Some studies try to minimise this risk by standardising the practitioner's interaction with participants, though practitioner effects may still be substantial in this setting (Kelley et al., 2009).

## Detection bias

Detection bias refers to systematic differences between groups in how outcomes are determined. The simplest example could be applying the follow up measurements to the two groups after different time intervals, allowing different amounts of natural remission. Also, assessments performed by an unblinded acupuncture practitioner would obviously risk introducing serious detection bias. Blinding of assessors helps to counter this, and blinding of patients for self-assessed subjective outcomes such as pain. Blinding of patients is an essential component of explanatory trials where the main outcome is a subjective measure of pain, since cognitive and emotional factors related to practitioner patient interactions and the therapeutic environment can have a powerful effect in their own right (see Chapter 7, section on Context Effects). Detection bias is a significant problem in 'open label' trials such as comparisons with waiting list or usual care alone. If patients score their symptoms themselves, they are likely to be influenced by gratitude for having received acupuncture, or disappointment at not receiving acupuncture. For example, it has been suggested that in those groups not randomised to receive acupuncture interventions within the large comparative RCTs that were part of the *Modellvorhaben Akupunktur* (Cummings, 2009a), called the GERman ACupuncture trials (GERAC) trials, there may have been a degree of resentful demoralisation. This would lead to worse outcomes reported in those groups. However, a counter to this argument is the Zelen design of Hinman et al. (2014), in which the control group that did not receive an acupuncture intervention was actually unaware of being measured as part of a trial. There was still a genuine effect of acupuncture measured in this setting, so detection bias from resentful demoralisation in open (usually pragmatic) acupuncture studies may not be such a strong argument.

## Attrition bias

Attrition bias refers to systematic differences between groups in withdrawals from a study. One significant risk is that non-responders may be more likely to drop out of the acupuncture arm,

which leads to an overestimate of the effect of acupuncture. Attrition may also be through exclusion, for example because of protocol violation. This is addressed by giving preference to analyses that include all randomised participants based on their original allocation no matter what intervention they receive, so called intention to treat analysis. While this analysis reduces bias, it also reduces statistical power; and clinicians are likely to be more interested in the effect on patients who actually received the treatment (the per protocol analysis).

## Reporting bias

Reporting bias refers to systematic differences between reported and unreported findings. There is a strong tendency to report only the outcomes where there are statistically significant differences between groups. This can be addressed by publishing protocols of intended trials, which commits the research team to the primary outcome and the method of analysis.

Reporting bias is not to be confused with publication bias, which refers to the tendency to publish trials with positive results over trials without positive results (sometimes referred to as negative, although most are inconclusive statistically rather than negative).

## Other biases

These are relevant only in certain circumstances: for example carry-over in cross-over trials; recruitment bias in cluster-randomised trials; and contamination, whereby the experimental and control interventions get ‘mixed’.

## Blinding in clinical trials of acupuncture

Blinding minimises various biases and should be considered for six classes of person involved in an acupuncture RCT: the participant, subject or patient; the acupuncturist or acupuncturists; any other care staff; the research team including any observers; anyone performing data entry and the statistician. For simplicity, and to focus on the special aspects of acupuncture research, this discussion will be limited to participant and acupuncturist blinding.

## PARTICIPANTS

Participants need to be blinded to minimise detection bias: blinding primarily serves to ensure that the effect of expectation related to either receiving or not receiving the intervention does not cause a systematic difference between the real and control groups. This is more important for ‘soft’ subjective outcome measures such as self-assessment of pain, as opposed to ‘hard’ objective outcome measures such as blood tests, imaging or pregnancy.

Naturally, participants cannot (usually) be blinded in studies where the control is no acupuncture, so-called ‘open label’ studies. The only substitutes for patient blinding in such studies are either the use of objective outcomes (e.g. pregnancy rates) or blinded assessment.

## ACUPUNCTURISTS

Acupuncturists and other care staff need to be blinded to minimise performance bias – consciously or subconsciously having a systematic influence on the patient’s score.

Blinding practitioners is obviously difficult to achieve while still maintaining an acceptable quality of intervention. There are needle devices (see in the following text) that can achieve blinding of the practitioner (Takakura and Yajima, 2007, 2008; Takakura et al., 2010), but whilst these are rather ingenious, their use will inevitably limit the scope of an acupuncture intervention.

## TESTING THE SUCCESS OF BLINDING

We would like to know if blinding is successful since it has such important implications on bias. This can be tested directly by asking patients to guess which group they were in, or indirectly by credibility ratings of the interventions. Neither method is perfect, but no other tools are available.

The logic of ‘credibility rating’ is that if the sham intervention is not significantly less credible than the real intervention, then it is assumed that blinding has been maintained. (This analysis of course is only valid with an adequate sample size; we know no RCT in which this has been considered.) The usual standard four questions include whether participants:

- are confident it can help their problem
- are confident in recommending it to a friend
- consider it logical
- and believe it would be successful in alleviating other complaints.

One potential problem with testing blinding is that the positive benefits of an effective treatment are likely to swing the assessment of credibility in favour of the real over the sham intervention. This can be reduced to some degree by testing credibility after only a few sessions, i.e. before it becomes obvious for the majority that there is a therapeutic effect.

## Study design

In the light of the above background information, the researcher’s remaining task is to make detailed arrangements for every aspect of the trial: including participants, intervention, control (the largest section here) and outcomes; or PICO. Lack of space means this chapter can only highlight some of the most common, obvious or interesting issues.

## PARTICIPANTS

In efficacy studies, participants should ideally have a single condition – to identify the effect of acupuncture on that condition. This leads to difficulties for example with ‘low back pain’ since most patients will have no pathological diagnosis. Acupuncture may not appear to have any specific effect overall (Cherkin et al., 2009), but may actually work for some patient groups (Sherman et al., 2009), the effect of which is lost in the overall group. It is usual to try to recruit a homogeneous group of patients who clearly have the condition in question, and no other condition. This leads sometimes to quite long lists of inclusion and exclusion criteria. In contrast, a pragmatic study often has far fewer criteria. In fact, pragmatic trials should exploit the one clear advantage of acupuncture over many other therapies – that it can be used safely in patients with multiple comorbidities.

Severity of the condition can be an issue that has to be carefully considered: patients with chronic, severe symptoms may only be helped by intensive combined approaches, if at all. By contrast, patients with mild symptoms may respond, but the change in scores is so small that very large numbers would be needed to show significant effects.

Participant recruitment can be problematic, for similar reasons. Patients responding to public advertisements are more likely to be the chronic, severe cases, and the same may be true of patients identified by searching practitioner databases. One possible solution is to recruit patients as they present with a condition to primary care for the second time a referral is considered. Their symptoms are likely to be severe ‘enough’ but not engrained.

The number that had to be screened to find eligible patients is an indication of the applicability of the intervention.

It seems clear clinically that some patients respond to acupuncture and others do not, probably due to genetic differences in the ease of expression of neurochemicals in the central nervous system. Unfortunately we have no way of identifying them beforehand, in order to recruit a favoured subpopulation for trials.

Explanatory trials of drugs use optimal doses in an ideal population (perhaps even a population that is pretested to be responsive to the drug). This is not the case for acupuncture trials. Dose is a difficult concept in acupuncture (White et al., 2008), and an ideal dose probably needs to be individualised to both the patient and the condition to some degree. To date, no clinical trials of acupuncture have preselected acupuncture responders, and anyway it is problematic: the patients will have experience of true acupuncture and therefore blinding would be more difficult.

## INTERVENTION

A fundamental challenge of acupuncture studies is deciding what is likely to be effective acupuncture for the group of patients recruited. The modes of action are increasingly understood in qualitative terms, but there is little evidence to determine the correct dose or schedule (White et al., 2008). Training and experience of individual acupuncturists vary widely but have to be set aside in carefully justifying the treatment.

Research reports often lay stress on the advanced qualifications of the acupuncturist providing the treatment, yet the evidence is clear that further training beyond an initial level does not improve outcomes (Witt et al., 2010).

## CONTROL

### No acupuncture controls

In pragmatic studies, the waiting list control group may be offered acupuncture after waiting until after the primary outcome is measured (e.g. 3 months in the ARC studies (Cummings, 2009a)). Disappointingly, their response to acupuncture cannot be used in the analysis since the comparison groups must be measured in parallel. The reason for this is somewhat theoretical: treatments given 12 months apart might have different effects because of extraneous factors, e.g. media reports of acupuncture, or socioeconomic changes. There are other problems: while it may appear ethical to give everyone the chance of acupuncture, in research terms the acupuncture given after waiting list is a waste of resources. Even worse, the design seriously risks detection bias: if acupuncture is presented as a ‘reward’ for waiting, it may be perceived as beneficial.

A challenging design is to compare acupuncture with another active treatment that is known to be superior to placebo. In a trial of 100 patients with migraine, there was little difference between acupuncture and valproic acid in terms of migraine episodes or use of rescue medication, though there were fewer episodes in the 6 months after acupuncture (Facco et al., 2013).

### Sham controls

In principle, the use of an inactive (placebo) control serves two purposes: it allows measurement of ‘specific’ effects, such as the effect of needle penetration; and it enables blinding of patients, minimising detection bias.

Blinding patients to the intervention in an acupuncture trial is in theory straightforward: both groups receive needling in some form. The research question in an explanatory trial of acupuncture in which both groups are needled tests the efficacy of one style of needling over another, rather than the efficacy of acupuncture as an intervention (Table 17.2).

The biggest problem in explanatory trials of acupuncture has been an inappropriate focus on the *sites* of needling, rather than the physiological stimulus given. Laboratory studies confirm that the strength of stimulus in sensory stimulation modalities is more important than the precise location of that stimulus (see Chapter 3), yet many clinical studies of acupuncture have compared needling at defined acupuncture points with needling a few centimetres away in the same muscle. This has been referred to as off-point needling, but we like to refer to it (with irony) as ‘missing

TABLE 17.2 ■ Features of different sham techniques used in acupuncture trials

Sham acupuncture techniques	Description	Comments
Off-point acupuncture	Acupuncture needling at points not generally used or described for acupuncture, i.e. away from (or 'off') classical points and meridians	Physiologically very similar or identical to real acupuncture
Wrong point	Acupuncture needling at acupuncture points not recommended according to acupuncture theory (usually TCM) for the condition studied	Physiologically very similar or identical to real acupuncture
Minimal needling	Very gentle subcutaneous needling, avoiding muscle stimulation with no attempt to elicit <i>de qi</i>	Active or partially active, depending on condition treated
Non-penetrating device (blunted cocktail stick, guide tube or finger nail)	Stimulation of skin either over or off classical points to simulate the insertion and sometimes the manipulation of a needle; often a similar technique is repeated to simulate removal of the needles	Can only be applied in areas invisible to the subject
Non-penetrating needle – standard	Simulated insertion of a real needle followed by taping of the needle to a point Insertion of a blunted needle through a foam cube stuck to the point	Can only be applied in areas invisible to the subject Real needling techniques through foam cube are limited
Non-penetrating needle – retractable	Streitberger needle – this needle is blunt and has a friction coupling inside a hollow coiled handle allowing the shaft to disappear inside the handle as it appears to penetrate the body; it is held in place by an adhesive plaster applied over a plastic ring Park sham device – this is made up of a combination of a retractable needle similar to the Streitberger needle with a guide tube of variable height attached to an adhesive base plate	Real needling techniques through adhesive plaster are limited; risk of skin penetration with blunt needle Real needling techniques through device are limited; areas limited to upward facing surfaces of subject to avoid placebo needle falling out of tube
Non-penetrating needle – double-blind	This device comes as a needle within an opaque guide tube, with both real and placebo versions; in the placebo version the needle is blunt and penetrates wadding in the guide tube; in the real version a needle penetrates the skin by 5 mm; the practitioner cannot tell the difference between the two during insertion	Real needling techniques limited to 5 mm insertion
Mock-TENS	TENS pads are used connected to an inactivated device or one set at a barely noticeable intensity level	Blinding may be considered inadequate
Sham laser	An inactivated low level laser device for performing laser acupuncture	Blinding may be considered inadequate

Most sham techniques appear to be active in comparison to usual care or no treatment controls. Comments in the third column of this table refer to theoretical physiological activity of needles rather than the whole treatment effects measured in RCTs.

the point', since in physiological terms the point (or idea) that should most often be tested is the strength of the stimulus rather than precise location of the needle stimulus (Cummings, 2001).

Too little emphasis has been placed on the physiological components of the intervention when designing explanatory studies in acupuncture, and too great an emphasis has been placed on traditional concepts, such as points and meridians, that have no clear physiological basis. Seeking to minimise bias, combined with this inappropriate adherence to non-physiological traditional concepts, has lead to results that appear to show that the better the quality (internal validity) of the trial, the more likely it is to be negative for acupuncture (Cummings, 2000; Smith et al., 2000). However, we would observe that the greater the authenticity of the sham acupuncture (the more reliably that bias is excluded), the more likely the interventions are to be the same in physiological terms, that is, two 'doses' of acupuncture are compared rather than real versus sham. This is nicely illustrated in the sensitivity analysis of the Cochrane review by Manheimer et al. (2010) on acupuncture for peripheral joint osteoarthritis.

**The evolution of sham techniques.** Off-point needling has been used as a 'placebo' or sham control in many explanatory trials of acupuncture. In studies with a low risk of bias there was little or no difference between the groups and often a moderately large change from baseline in both groups (Mendelson et al., 1978). So the next development was to reduce the 'dose' in the sham group but maintain adequate blinding. This was achieved by using superficial needling off-point in the sham groups, avoiding *de qi*. These studies also rarely demonstrated a significant difference between real and sham groups, and continued to show reasonable effects in the sham groups (Haake et al., 2007; Linde et al., 2005), although the effect size did appear to be different for different conditions – greater for central pain conditions such as migraine, and less for more peripheral pain conditions such as osteoarthritis of the knee, with chronic low back pain in between (Cummings, 2009a).

In 1998, Streitberger and Kleinhenz introduced a 'placebo needle' into acupuncture research (Streitberger and Kleinhenz, 1998) and proceeded to successfully demonstrate the superiority of real acupuncture in rotator cuff tendonitis (Kleinhenz et al., 1999). This 'placebo needle', now commonly referred to as the Streitberger needle, looks identical to a real needle, but has a blunt tip and a shaft that slides into the handle. This was seen by many as the solution to the problem of controls and blinding in explanatory studies of acupuncture, but unfortunately, in practice these needles continued to demonstrate substantial mean group effects from baseline. Moreover, the blunt needles occasionally penetrated the skin (Streitberger and Elden, personal communication). Streitberger needles have been found to have the same sensory impact, including *de qi* scores, as real needling in 60 volunteers (Xie et al., 2013).

This strong stimulation is partly derived from having to insert the blunt needle through an adhesive plaster stuck over a plastic ring at the site of insertion, so that the both real and sham needles stand in position after 'insertion'. An alternative device (the Park sham device (Park et al., 2002)) avoids this by using a guide tube with an adhesive plastic footplate, but this device has other limitations, that is the skin surface for application must be facing above the horizontal so that the sham needle does not fall out. In both cases, real needles are also inserted via the same method, which limits needle manipulation, and would make precise needling of trigger points impossible.

A further evolution of sham devices leads to the development of the so-called 'double-blind placebo needle'. This device comes as a needle and guide tube combination, some with real needles that can penetrate skin, etc., and some with blunt needles that penetrate stuffing within the tube and just touch the skin surface (Takakura and Yajima, 2007). This device has been found to successfully blind both the practitioner and the patient (Takakura and Yajima, 2008; Takakura et al., 2011), but it has been validated using rather fine needles (0.16 mm diameter) with limited penetration depth (5 mm). There would also be some limitation in the use of EA, since adequate stimulation would be associated with muscle twitch in the real group, and this would unblind the practitioner.

Various other controls have been used in sham-controlled trials of acupuncture, such as mock-TENS (White et al., 2004) and dummy laser (Irnich et al., 2001). These are clearly not needle acupuncture, but if the population is sufficiently naïve to acupuncture techniques, it may be possible to achieve blinding sufficient to minimise detection bias.

One of the simplest techniques is to use non-needle devices, such as the pointed fingernail (Junnala, 1983) or blunted cocktail sticks (Cherkin et al., 2009; White et al., 1996), which appears to be remarkably successful at achieving blinding. Unfortunately such interventions within the context of an acupuncture trial have also performed remarkably well, suggesting that in some settings the context of care surrounding acupuncture has a rather larger influence than the specific effect of the intended needle stimulus.

### How active is sham acupuncture?

We must accept that the sham technique is likely to be partially active, although the effect size of this intervention may vary considerably depending on the condition treated, based on the observation that some patient populations are more sensitive to sensory stimulation techniques than others. It is impossible to measure the specific effect of sham acupuncture, since we have no potential for a blinded control group. So all we can do is to estimate the change from baseline (including both specific and non-specific effects), or make measurements against unblinded comparators, such as usual care or guideline based conventional care.

In an extensive meta-analysis, Linde et al. (2010b) compared the size of the effect of sham acupuncture with that of no acupuncture controls. They included 37 trials and found a pooled effect (standardised mean difference – SMD) of 0.45 in favour of sham over no acupuncture controls. For comparison, the SMD of pharmaceutical placebos is estimated to be around 0.1 against no treatment. Linde et al. went on to discuss that if the effect size of acupuncture in clinical trials is 0.4 or more (SMD) for non-specific effects and 0.2 or less for specific effects, then to achieve 80% power, a two-armed, sham-controlled clinical trial would have to recruit about 800 patients. This suggests that almost all trials comparing true and sham acupuncture to date have been underpowered.

### Can the observed difference between effects of real and sham acupuncture be attributed to bias?

In 2009, Madsen et al. found, in a meta-analysis of three armed studies of acupuncture in pain conditions, that the specific effects of acupuncture over sham acupuncture were statistically significant (SMD  $-0.17$  (95% CI  $-0.26$  to  $-0.08$ )). However, the authors suggested that the effect was clinically irrelevant and could not be distinguished from bias from unblinded practitioners (Madsen et al., 2009). They failed to acknowledge that the effect of acupuncture compared with no acupuncture controls was clinically relevant (White and Cummings, 2009). They also failed to explain the mechanism whereby an unblinded practitioner could influence the outcome of a trial when the patients or outcome assessors remained blind to treatment allocation – or provide evidence that such an effect exists, other than as a theoretical possibility. Unfortunately this dismissal of the small but highly statistically significant superiority of real acupuncture over sham has been repeated in other reviews and guidelines without proposing a plausible mechanism for the alleged bias.

The first individual patient data meta-analysis in acupuncture for chronic pain was performed by Vickers et al. (2012), and this demonstrated highly significant differences over sham acupuncture and over no acupuncture controls (most of which involved active treatment, but just no acupuncture). The difference over sham was again small at around an SMD of 0.2, and the difference over no acupuncture controls was larger at around an SMD of 0.5.

## OUTCOME

The effects of the interventions are evaluated with appropriate measures that have to be applied at appropriate time points.

In many conditions there are standard outcome measures that are valid and reliable and sensitive to change – the essential requirements. These should of course be used for studies of acupuncture as of other treatments. But it is recommended to also use QoL measures to try to capture other more general health benefits of acupuncture. The EQ-5D has a special place as its scores can be used to assess cost-effectiveness, although one of the subscales of the SF-36 can also be used. We must bear in mind, however, that it is important to avoid overburdening participants with too many outcome measures.

Although pain severity is a common outcome measure for musculoskeletal pain conditions, severity is not always the most relevant outcome to measure. For example, patients with headache are more concerned to have an extra day free of headache per week than to measure a 25% reduction in the pain severity. Also, in conditions where pain is expected and analgesic drugs provided, such as labour and following surgery, pain levels are unlikely to be reduced by acupuncture – though the use of alternative analgesic techniques or analgesic drugs is very likely to be lower (Ntritsou et al., 2014; Vixner et al., 2014). Careful consideration of the most appropriate measure is important, since the ‘primary’ measure has to be nominated before data collection starts, and changing it later is clearly open to bias. For example, Kotani et al. (2001) designed their trial to measure supplemental opiates rather than pain scores for postoperative pain: indwelling dorsal segmental needles caused a significant difference in drug dose, but not in pain scores.

It is also important to follow patients up for a relevant time, depending on the condition. For example, many studies of acupuncture for weight loss end after 6 weeks. Although many are positive, they have little clinical relevance for a condition that is essentially life-long.

## Concluding comments

In this chapter we have defined the terminology of RCTs, and described the formulation, design and interpretation of RCTs as these aspects relate to research questions about acupuncture. We have focussed on the difficult issues of blinding and controls within explanatory research and emphasised the issue that most sham acupuncture techniques are associated with notable effects in clinical trials as compared with pharmaceutical placebos or non-acupuncture controls. We have noted that the major issue in interpretation of clinical acupuncture research is the misguided attribution of clinical significance to the difference between real acupuncture and sham techniques rather than to the more pragmatic comparisons with usual care or conventional alternatives.

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# A critical approach to systematic reviews of acupuncture

A. White

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## Introduction

A systematic review 'attempts to answer a specific research question by assembling and then analysing all the relevant evidence' (modified from Cochrane Handbook, <http://handbook.cochrane.org>). One big threat to finding the 'true' answer is the reviewer's bias, so every step of the review is designed to reduce bias.

- A clearly stated set of objectives with predefined eligibility criteria for studies;
- An explicit, reproducible methodology;
- A systematic search that attempts to identify all studies meeting the eligibility criteria;
- An assessment of the validity (critical appraisal) of the included studies, for example through the assessment of risk of bias; and
- A systematic presentation and synthesis of the characteristics and findings of the included studies.

Systematic reviews can be used for a wide range of research questions in acupuncture, such as cost effectiveness (Kim, S. Y., et al., 2012), safety (Xu et al., 2013), wider topics such as 'Acupuncture pain research in Australia' (Zheng and Xue, 2013) or use in particular settings such as emergency departments (Kim et al., 2013). But they excel at testing effectiveness because they can pool results from studies that are individually too small to provide definitive answers. This is particularly critical for distinguishing small differences, such as between the effects of real and sham acupuncture, which has been estimated to require a sample size of 800 (Linde et al., 2010).

Reviews of acupuncture's effectiveness are the focus of this chapter. They often use a *meta-analysis*, which is a statistical method for pooling and summarising the results of independent studies. A meta-analysis provides more precise estimates of the effects of health care than any individual study, and is recognised as the highest level of evidence that can guide choices in health care (Sackett et al., 1996).

### Clinical points

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Turning evidence into guidelines or recommendations for practice involves three steps: (1) synthesis/summary, in a systematic review (2) interpretation (3) consideration of the healthcare context.

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Positive evidence from a systematic review does not automatically determine the policy on whether to recommend a treatment or not. The strength and relevance of the evidence have to be thoughtfully considered in interpreting it for patient care, and set in the context of other available treatments. And, before finally adopting a therapy, the evidence has to be considered in relation to other factors according to the context in which it could be applied. For public policy this is a decision for the guideline group, not the reviewer. Costs, availability of other therapies and trade-offs between benefits and costs have to be taken into account.

Like public policy, information provided to patients in leaflets or websites should be based on the highest level of evidence (Bishop and Salmon, 2013). But not all healthcare decisions have to be made with this high level of rigour. Individual practitioners make clinical decisions by combining the formal evidence with their own clinical judgement and their patient's preference. Individual patients may base their decisions on what other patients say rather than on formal published 'evidence', knowing that such evidence reflects only the average effect on groups, not the response of an individual patient (Segar, 2012). They may view a lack of evidence as failure of the scientific method properly to evaluate the treatment they know is effective; or that simply not enough has been done yet to be overwhelmingly positive.

### Clinical points

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Bias: 'any process at any stage of the inference which tends to produce results or conclusions that differ systematically from the truth' (Sackett, 1979).

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Bias, both in the original studies and in the review itself, is the major concern when evaluating evidence. Bias cannot be completely excluded and can seriously influence a study's results. A review that generates a result with narrow confidence intervals may appear convincing, but readers should be alert to the possibility of bias. In most reviews the bias favours acupuncture, but reviews may also be biased against acupuncture.

Unfortunately, the very process of achieving rigour in a review makes the process more complex, and may mean that the published report can become obscured by specialised terms and concepts. Increased rigour can mean reduced accessibility. Reviewers have to work hard to make their reports accessible.

### Clinical points

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Checking the facts behind a systematic review's abstract is crucial but not always simple.

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Reviewers of acupuncture trials face additional challenges, discussed in this chapter, such as the complexity of clinical effects; incomplete knowledge of mechanisms; uncertainty about adequate treatment; and the absence of convincing but inactive controls. The inventions of the word processor and meta-analysis software appear to make a systematic review an 'easy' project that can be completed without leaving the desk or having to recruit patients. As a result, reviews are

sometimes done by authors with no deep understanding of either acupuncture or the condition they are writing about. Such reviews may be ‘technically’ adequate, yet may not deal with the particular challenges of acupuncture. The proliferation of ‘word-processed reviews’ on topics where the evidence was obviously inadequate at the outset can give the public a false impression of ‘yet another negative review’ on acupuncture.

## NARRATIVE REVIEWS HAVE A ROLE

Before the 1990s, experienced clinicians wrote narrative reviews based on their clinical impressions, citing the papers that supported their views. While a ‘systematic’ approach to including and appraising studies is a huge step forward, we should recognise that there is still value in an experienced clinician writing a thoughtful review of the evidence, rather than mechanically analysing ‘effectiveness’ alone. In many conditions, acupuncture research is not yet mature enough to justify systematic reviews of effectiveness. Thoughtful ‘systematic narrative reviews’ can usefully summarise the evidence and guide both current practice and future research.

### Clinical points

The proliferation of inconclusive reviews feeds the prejudices of acupuncture’s detractors: ‘Another negative study on acupuncture’.

Using the literature on weight loss as an example, one review found some evidence for an effect of acupuncture on body weight (Cho et al., 2006), but was inconclusive. A much broader, narrative review by a team of clinicians was able to consider the evidence ‘in the round’ including possible mechanisms from both animal studies and human studies (Belivani et al., 2013). The latter authors discussed acupuncture’s effects on leptin and ghrelin metabolism, and considered that EA seems more promising than body or auricular acupuncture, and recommended that combinations of acupuncture, exercise and diet should be studied.

## ESTIMATES OF ‘EFFECTIVENESS’

The results of a meta-analysis may appear in various formats, shown in Table 18.1. This chapter uses two: *standardised mean difference* (SMD) when a symptom such as pain is measured on a scale and *relative risk* (RR) when the response is divided into Yes or No (such as quitting smoking).

This chapter frequently uses the concept of SMD because this expresses the ‘effect size’ (ES) of a therapy. The concept of ES is intuitive, although the values that it is expressed at are not. To be strictly accurate, there are a number of different ways of calculation the ES, and we are referring here to Hedge’s ES, i.e. the effect divided by the standard deviation (SD). While the meaning of different values of ES is much debated, Table 18.2 presents some commonly used values.

## EVALUATING SYSTEMATIC REVIEWS

Formal methods for evaluating the quality of systematic reviews exist. The PRISMA guidelines (Preferred Reporting items for Systematic Reviews and Meta-analyses) (Moher et al., 2009) consist of a 27-item checklist for conduct and reporting. A good tool for specifically assessing bias in a review is the checklist (Shea et al., 2007) of 11 items ranging from design to conflict of interest.

However, the aim of this chapter is to provide a more informal way of suggesting how readers can approach a review, section by section. The chapter will also discuss the special techniques of individual patient data meta-analysis and network meta-analysis (NMA). The chapter is presented in the sequence in which a review is read, making it easier to find the relevant section. It does

TABLE 18.1 ■ Different methods for expressing the pooled results as a single value

Method	Used when	Calculation	Value for 'no difference'	Units, interpretation
Mean difference	All studies used same measure (e.g. pain VAS)	Simple mean	0	Same as the original measure; 'large' effect may be 33% or 50% difference
Standardised mean difference	Studies used different measures for the same symptom (e.g. WOMAC* pain, Lequesne index)	Express relative to SD	0	Measured in SDs; i.e. ES. Large ES is >0.8 difference
Odds Ratio	Yes/no response	Successes/failures	1.0	Odds, as in betting (no simple interpretation)
RR	Yes/no response	Successes/total	1.0	Chance of response (RR 1.6 means 60% greater chance)

\* WOMAC, Western Ontario and McMaster Universities Arthritis Index

TABLE 18.2 ■ Effect sizes corresponding to clinical effects

Clinical effect	Effect size (or SMD)
Small	<0.3
Moderate	0.3–0.5
Large	>0.5

not aim to be comprehensive, and further information can be found in the Cochrane Handbook (<http://handbook.cochrane.org>).

## Defining the research question

First, look for a clear, well-defined research question. This should be found at the end of the 'Introduction' section or beginning of the 'Methods' section, or as an 'objective' in a Cochrane review. Authors typically use the memorable PICO (participants, intervention, control, outcome) format.

Authors do not always identify *all* the relevant research questions. For example, the first three versions Cochrane review of acupuncture for smoking cessation only considered courses of separate sessions of acupuncture, ignoring the fact that some studies also used sustained auricular stimulation between sessions. At the fourth revision, one author commented that sustained stimulation might have an effect of its own. So a new analysis was done and found to be positive. (White et al., 2014) The dilemma was then how much weight to put on this *post hoc* analysis; the interpretation was very cautious because the analysis was not prespecified.

### Clinical points

Was any <i>post hoc</i> decision rational? And did it minimise risk of bias?
--

Authors should also prespecify the type(s) of study they will include, often limited to randomised controlled trials.

## PARTICIPANTS

Look for a definition of the types of patients included and the setting (primary or secondary care). This should state the medical condition precisely, and perhaps the particular group at interest – such as shoulder injury following stroke (Lee et al., 2012).

In a perfect world, a predefined question defines every step of the review and anticipates every problem. In reality, decisions crop up that were not anticipated, for example if a trial report is ambiguous. Authors must make these decisions in a way that removes their inbuilt bias – for example, by deferring to a (blinded) third party. Readers should be particularly on the lookout for decisions that were made *post hoc* (after seeing the data).

## INTERVENTION

Acupuncture comes in diverse forms, and readers should look for a clear definition that dictates which studies to include. The decision about what is and is not ‘acupuncture’ would have a firmer basis if we had more precise knowledge of the mechanisms of acupuncture in various conditions.

### Clinical points

Check what the reviewers mean by ‘acupuncture’.

Some reviewers specifically limit themselves to one approach: Manheimer et al. (2010) considered only ‘traditional acupuncture’ and excluded a study of periosteal needling (Weiner et al., 2007). But other authors (Lam et al., 2013) defined traditional acupuncture theory as ‘... classical meridian points, trigger points, ear points, or painful points, regardless of the stimulation source’ which seems a sensible compromise. Yet others combine all forms of stimulation, for example PC6 (Lee and Fan, 2009).

## CONTROL

Choice of the comparator for acupuncture trials is a thorny issue (see Chapter 17): basically, trials use either some form of ‘pretend’ acupuncture as a placebo, or no acupuncture – either just waiting list, or with some other treatment. Acupuncturists feel challenged by its common dismissal as ‘just a placebo’, so there is pressure to compare acupuncture with ‘placebo’ of some sort. This has stimulated great inventiveness with sharpened finger-nails, cocktail sticks and plastic tubes, all of which might be active and so are better called ‘sham’.

Many trialists have combined two questions into a single, three-arm study for efficiency. The first such trial was probably reported in 1993 (Spratt et al., 1993); the design was made famous by the *Modellvorhaben* series (Cummings, 2009).

But many formal reviews define three questions separately:

- Acupuncture effective compared with sham acupuncture?
- Acupuncture effective compared with usual care?
- Acupuncture effective compared with another active treatment?

## Outcomes

Authors of effectiveness reviews are usually pragmatic and preselect the outcomes that they know the primary studies have used. Otherwise, they may have no studies to analyse. This almost happened with the Cochrane Review of acupuncture for Bell’s palsy, which prespecified ‘incomplete recovery at 6 months’. Eight potential studies were located, but none used this outcome (Chen et al., 2010). A subsequent review using a simpler ‘response rate’ included all eight RCTs – though the result was inconclusive because of risk of bias (Kim J.-I., et al., 2012).

Ideally, reviewers should also extract any data on safety that is reported in clinical trials, and include a narrative review of safety in their final summing up.

## Gathering the data

The process of collecting data for the analysis involves conducting searches, selecting appropriate studies, then extracting data on outcomes, risk of bias and acupuncture adequacy.

## FINDING AND SELECTING STUDIES

Searches for acupuncture are challenging since some studies are likely not to be indexed in the usual databases, but only in the ‘grey’ literature (such as doctoral theses) and in the non-English language literature. A review that is truly ‘comprehensive’ should search all known databases without language restriction.

The increasing maturity of the research community in East Asia means that Chinese and Korean databases are regularly included. The former reluctance to include Chinese language studies was based on the common risk of bias – unclear randomisation processes, and outcomes not assessed blind, and results were universally positive (Vickers *et al.*, 1998) until the turn of the millennium. Clearly, all trials that meet certain standards must be included.

### Clinical points

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Check that the review does not ‘cherry-pick’ the studies that match the authors’ opinions.

---

## EXTRACTING DATA

It can often be surprisingly difficult to extract reliable data from the published report even on such basic matters as numbers of participants and symptoms scores. So data should be doubly extracted or independently checked. Other challenges include converting data from one score to another and calculating SDs, but these are beyond our scope here.

Crossover designs present a dilemma; this design is usually efficient in sample size since patients are used as their own controls, minimising the variability between the two arms. However, acupuncture may have long-term effects that carry over into the second phase, so there will be significant movements in the baseline measurements. Blinding in the second arm may be difficult. For these reasons, it is common to extract data from only the first phase.

### Risk of bias (also known as ‘Quality’) of trials

Reviewers must assess the risk of bias in the clinical trials which means its scientific rigour, or ‘internal’ validity (which is different from ‘external’ validity – its relevance to normal clinical practice). Risk of bias used to be called ‘study quality’, but this is a value laden term that is better avoided.

Checklists were introduced to try to provide a single score for bias. The Jadad score (Jadad *et al.*, 1996) was attractive because it was formally validated, but is unreliable and now rarely used (Juni *et al.*, 1999). A more transparent process has been developed, the Cochrane ‘assessment of risk of bias’, shown in Table 18.3 with examples.

### Blinding

Different reviews assess risk of blinding of participants in different ways. Some are satisfied if blinding is designed into the study. Others demand that blinding is verified, either indirectly by demonstrating that there was no difference between the ‘credibility’ (e.g. ‘How confident were you that the treatment would be effective?’) of the two interventions or directly (Which group do you think you were in?). Blinding may not be perfect, but asking participants is also not perfect as they may be influenced by their response to treatment.

TABLE 18.3 ■ Risk of bias criteria, and examples

	Text extracted or summarised
Adequate sequence generation	'Balanced randomization' no further details <sup>a</sup>
Allocation concealment	'Random list was openly accessible to the physician enrolling the patient'
Blinding	'No blinding'
Incomplete outcome data addressed	'33 of 160 dropped out; reasons were not reported; no intention-to-treat analysis'
Free of selective reporting	'Visual analogue scales were used but only global responder measures are reported'
Other threats to validity	'Significant differences between groups at baseline'

<sup>a</sup>Classified as 'unclear' risk; other examples classified as 'high' risk.

Reviews should apply the risk of bias, often to the analysis itself by excluding studies below a certain arbitrary threshold in a sensitivity analysis. In any case, the interpretation of the results has to take account of the risk of bias.

Clinical points

Check that the review assesses risk of bias and then applies the findings.
--

Assessing adequacy of acupuncture

Reviews that include studies that used inadequate acupuncture underestimate acupuncture's effectiveness. The challenge is in defining 'adequate' with incomplete knowledge of mechanisms, particularly of the differences between real and sham.

Various methods have been used to assess adequacy: judgement from clinical experience (Linde et al., 2009a) to rate each study for how similar would the reviewers' own treatment be and confidence that the acupuncture would be adequate. Another method is to assess trials for choice of points, number of sessions, needling technique and acupuncturist's experience (Furlan et al., 2005). However, this method may be unreliable as scores changed between two versions of one review (Manheimer et al., 2007, 2010).

Clinical points

Check that the review evaluates 'adequate' acupuncture.
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Another review used objective criteria for treatment of knee OA (White et al., 2007): studies had to use at least four points, stimulated needles by hand or EA, and gave at least 6 treatments at least once a week. Other studies were excluded from the analysis, though more often a subgroup analysis compares groups of studies that do or do not meet a particular criterion such as a minimum of six treatments (Manheimer et al., 2010).

Analysing the data

This section focuses on how the meta-analysis is organised. The challenge is not in the statistical procedure – which software makes simple – but in deciding whether, when and how to combine studies. Combining increases the power but may introduce bias, may miss effects in subgroups, and may provide an answer to a question that is not clinically relevant.

# DIVERSITY AND HETEROGENEITY

We use the terms diversity and heterogeneity here in the way preferred by the Cochrane Handbook. *Diversity* means differences in the way studies were conducted, and this may result in *heterogeneity* in their results.

- Clinical diversity – different techniques of acupuncture or type of participant
- Methodological diversity – different design, for example control groups (sham, usual care, another treatment), or different outcomes (pain, function) and different time points
- Statistical heterogeneity – the studies’ results vary more than would be expected from random variation (chance). This is caused by clinical or methodological diversity. For simplicity, we refer only to the  $I^2$  statistic to measure heterogeneity, and regard any value of  $I^2 \geq 30\%$  as indicating moderate heterogeneity, and  $\geq 50\%$  substantial.

To illustrate diversity between studies, some examples are tabulated in [Table 18.4](#).

Reviewers operate between two extremes: at one end, they can form groups of very similar studies – ending up with an unwieldy number of analyses each with too few studies. Or they can combine all the studies into a single analysis, addressing a very general, or even meaningless, question with high confidence. Readers should note what was done and consider whether it addresses the question they are interested in.

## Clinical points

Check how a review deals with diversity between studies.

## Primary analysis: lumping or splitting?

Combining all studies, known as ‘lumping’, has the benefit of statistical power. One might argue particularly against lumping studies that use different control groups because they are addressing fundamentally different research questions. But even this argument can be countered: it seems in principle highly unlikely that the results of studies comparing acupuncture with sham acupuncture (for example) will be all on one side of the midline, and those comparing it with usual care (for example) on the other side. Patients want effective treatments, so all available data should be used in making that decision. This suggests that it is legitimate to combine all RCTs, whatever their control groups, to test the overall effect of acupuncture.

It seems likely that lumping provides answers about acupuncture for individual patients and their practitioners, whereas public health policy decisions are more likely to be made on comparisons with sham. The decision to lump or split relies on common sense and a good understanding of the research question. Readers should be aware of what has been done. One solution is to lump first and split afterwards by means of a subgroup analysis, described later.

TABLE 18.4 ■ Examples of clinical and methodological diversity in acupuncture studies

Study component	Examples where diversity may arise
<b>Clinical diversity</b>	
Participants	Medium or severe symptoms at baseline
Acupuncture approach	Points; stimulation; treatment schedule
<b>Methodological diversity</b>	
Co-intervention	Physiotherapy; medication; none
Type of control	Sham needling; usual care; other active intervention
Outcome type	Symptom; function; quality of life
Outcome timing	End of treatment; long-term follow up

Random or fixed effects analysis?

Meta-analysis software offers two kinds of analysis – fixed effects or random effects. Many authors use fixed effects when there is no heterogeneity and random effects analysis when there is. Others argue this is a misunderstanding. The debate about which is most appropriate is beyond this chapter’s scope, happily for the reader. Both have their supporters. Readers can be most reassured when both methods are used, and the more conservative result is adopted.

A technical argument against combining acupuncture studies notes that diversity leads to heterogeneity, so reviewers use random effects: but the diversity also means that the assumptions justifying this analysis are rarely met! (Prady et al., 2014).

SECONDARY ANALYSES

Two types of further analyses will be discussed: one (sensitivity) mainly used to examine the robustness of the primary analysis, the other (subgroup) mainly to explore reasons for heterogeneity and secondary research questions.

Sensitivity analysis

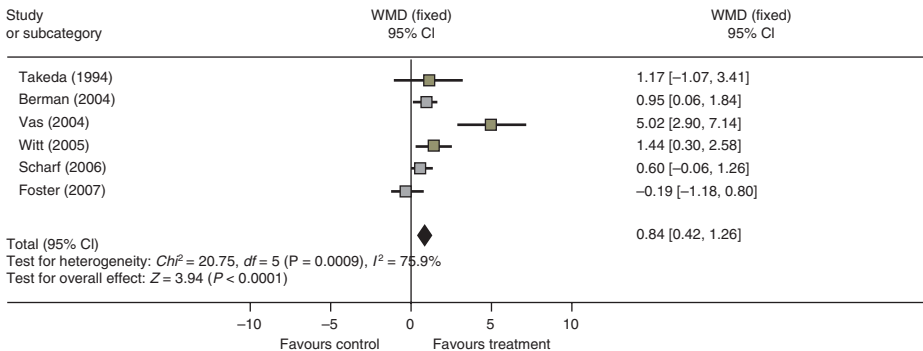
The purpose of a sensitivity analysis is to test whether the results are robust, or whether they rely too heavily on potentially questionable data – such as studies with significant risk of bias, or with heterogeneous results. The analysis is run again without the potentially questionable data.

One particular example of this process is rather contentious, involving sham-controlled studies by Vas and colleagues (Vas et al., 2004, 2006, 2008). Their results are significantly more strongly positive than most, and lead to heterogeneity (Figure 18.1). Two meta-analyses (Vickers et al., 2012; White et al., 2007), excluded them in a sensitivity analysis because they were ‘outliers’. Without them, the remaining results were free of heterogeneity.

It can be argued that in this case the sensitivity analysis diverts attention from the most important finding – that treatment techniques of Vas, with deep needling and strong EA stimulation, are more effective and should be recommended. Moreover, these studies are at low risk of bias. The counter-argument is that these studies are so different that they threaten the validity of the analysis, but demonstrating that the result remains positive without them sends a powerful message.

Subgroup analyses

The example earlier suggested that the greater effect seen in one study (which caused the heterogeneity) might be due to one particular aspect of treatment, such as use of EA. This can be tested



**Figure 18.1** Meta-analysis of acupuncture for OA knee pain showing one clearly outlying result leading to significant heterogeneity. WMD, weighted mean difference.

in a subgroup analysis in which studies are sorted into two subgroups (manual and EA) and their results pooled and compared.

Great caution is needed in interpreting subgroup analysis: the result could be an important finding that influences the choice of treatment – or it may be a spurious, chance finding that is totally misleading. Experts are nervous (Sun et al., 2010). After all, the participants were not randomised into the groups given manual or EA – the comparison is ‘indirect’. Also, the two groups of studies are likely to differ in other ways – setting, rigour, types of patient and so on.

## Clinical points

Check that reviewers interpret subgroup analyses cautiously.

Readers should be cautious of subgroup analyses. They should be specified beforehand, based on biological rationale, and consistent across different outcomes: and other formal tests are available (Sun et al., 2010). It is safer to regard subgroup analysis as suggesting a new hypothesis to be tested in a new RCT, rather than conclusive. Thus, in 16 RCTs of acupuncture for OA pain, Manheimer found four studies using EA showed larger effects (SMD 0.05 CI 0.20, 0.81) than the five that did not (SMD 0.11, CI −0.07, 0.29). The result was correctly labelled hypothesis generating, not confirmatory.

In one early, comprehensive review acupuncture, Ezzo and colleagues analysed 51 RCTs in chronic pain (Ezzo et al., 2000). In a subgroup analysis, RCTs using more than six sessions of acupuncture showed a greater effect on pain reduction than those with less than six ( $p < 0.03$ ). This finding should stimulate further research but should not be regarded as conclusive.

## Meta-regression

Meta-regression is more sophisticated than subgroup analysis but serves a similar purpose, i.e. testing a study characteristic that might be associated with larger effects. It can use continuous data like number of needles, not just dichotomous data (like use of EA or not), and it can take into account other differences between studies.

Meta-regression usually consists of two steps. First, the effect of each individual difference is tested one by one, such as sample size, number of points used and number of treatments given. The most positive is then selected and analysed while taking account of the others. While more reliable than subgroup analysis, this method can only deal with factors that are known, so still risks finding false positives. It requires at least 10 studies for every feature analysed.

In one example, meta-regression was performed on the 29 low-bias pain studies for which individual patient data were available (MacPherson et al., 2013). The authors tested whether certain features of the acupuncture technique (Box 18.1) influenced the outcome. The analyses were negative for all the factors tested, except the number of needles used and number of sessions given – both associated with increased effects. Any conclusions from these results have to be cautious in view of the number of tests carried out.

### BOX 18.1 ■ Treatment factors examined in meta-regression (MacPherson et al., 2013)

Style of acupuncture  
Point prescription, location of needles, number of needles used  
*De qi*, and use of EA or moxibustion  
Therapist experience and permitted interactions  
Number, frequency and duration of sessions

TABLE 18.5 ■ Effect sizes in 29 studies (Vickers et al., 2012)

Pain location	N, vs. sham	N, vs. non-acupuncture control
Spine	8, 0.37 (0.27, 0.46)	7, 0.55 (0.51, 0.58)
Osteoarthritis	5, 0.26 (0.17, 0.34)	6, 0.57 (0.50, 0.64)
Chronic headache	4, 0.15 (0.07, 0.24)	5, 0.42 (0.37, 0.46)
Shoulder pain	3, 0.62 (0.46, 0.77)	0

Values are number of studies, SMD and CI.

## INDIVIDUAL PATIENT DATA META-ANALYSIS

Most meta-analyses use data from patients in the form of a group mean and SD. These data are not without flaws: some data are missing, some have been substituted in various ways. The precision of the analysis can be increased by using original data on individual patients. One landmark study of acupuncture included 29 studies with 17 922 participants – only those studies where randomisation had been concealed, to minimise risk of bias (Vickers et al., 2012).

The results (Table 18.5) show an overall ES of acupuncture compared with no acupuncture of about 0.5, or ‘moderate’. There was heterogeneity in the comparison that was explained by effects of co-intervention such as exercise.

Sensitivity analyses showed that the result was robust to risk of bias, small sample size and heterogeneity. Authors estimated it would take 47 studies with 100 patients showing an effect of sham over acupuncture of 0.25 to reduce the ES to zero.

### Clinical points

‘Acupuncture is a reasonable referral option for patients with chronic pain’ (Vickers et al., 2012).

## Network meta-analysis

One set of trials compares drug A with placebo; another set of trials compares drug B with placebo. But no trials compare A and B directly. A ‘NMA’, or multiple treatments analysis, is designed to do an indirect comparison of A and B.

With acupuncture, the main challenge is that sham acupuncture should not be considered equivalent to placebo pills. This misunderstanding occurred in the NICE guidelines on treatment of headache (NICE, 2012) which used a NMA to compare acupuncture compared against sham with four different drugs for migraine prophylaxis, all tested separately against placebo pills. Although this misunderstanding underestimated the effect of acupuncture, the evidence was still strong enough for it to be recommended.

## NMA OF ACUPUNCTURE FOR OSTEOARTHRITIS

Corbett and colleagues conducted a NMA of physical treatments for knee OA pain, and appropriately analysed sham acupuncture separately from placebos (Corbett et al., 2013). Table 18.6 shows the primary analysis of all studies. A second analysis of 42 better quality trials showed acupuncture to be more effective at reducing pain than sham acupuncture, muscle-strengthening exercise, weight loss, aerobic exercise and no intervention.

### Clinical points

Moderate evidence: acupuncture is one of the most effective conservative interventions for knee OA pain.

TABLE 18.6 ■ NMA of various interventions compared with standard care for knee osteoarthritis pain: end of treatment change in pain

Intervention	Studies, SMD (95% CI)
Acupuncture	24, 0.89 (CI 0.59, 1.18)
Balneotherapy	9, 0.65 (CI 0.15, 1.04)
TENS	12, 0.65 (CI 0.25, 1.06)
Aerobic exercise	11, 0.55 (CI 0.21, 0.89)
Sham acupuncture	14, 0.47 (CI 0.09, 0.84)
Muscle-strengthening exercise	28, 0.40 (CI 0.19, 0.61)
Weight loss	5, 0.26 (CI −0.15, 0.67)
No intervention	5, −0.44 (CI −1.04, 0.15)

## Interpreting the data

So far we have discussed the steps of the review up to finding a result, such as a certain ES for particular outcomes, against particular comparators. Authors who finish there and immediately ‘recommend acupuncture as a treatment for condition X’ are overly optimistic, missing out two vital further steps: evaluating the quality of the evidence (part of the review’s Discussion) and making recommendations (the role of guideline groups).

### Clinical points

Turning evidence into recommendations involves three steps: synthesis/summary; interpretation; consideration of the healthcare context.

Systematic reviews synthesise and summarise the evidence (in the ‘Results’ section) and then should thoughtfully evaluate its quality (amount, certainty and risk of bias) in the ‘Discussion’ section before reaching a ‘Conclusion’. They should rarely make any recommendation to implement the treatment – that depends on costs and priorities which are in the political, not research, arena. The only exception could be when acupuncture is shown to be effective and safe, and can be introduced at no additional cost or inconvenience. The most that a review should do is conclude that acupuncture ‘could be considered’. It should however make recommendations for further research.

As a formal method of evaluating the quality of evidence, GRADE (Grading of Recommendations Assessment, Development and Evaluation) is now widely used and is briefly introduced here. Then an informal checklist is presented with some examples from acupuncture reviews.

## GRADE APPROACH TO QUALITY OF EVIDENCE

The GRADE method will be discussed in simplified terms, and only as applied to evidence from RCTs. Using predetermined criteria, it allocates the body of evidence to one of four categories:

- *High quality* – Further research is very unlikely to change our confidence in the estimate of effect
- *Moderate quality* – Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
- *Low quality* – Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
- *Very low quality* – Any estimate of effect is very uncertain

Evidence from RCTs starts off as ‘high quality’, and for each criterion that it fails, its quality status is downgraded by one level. Table 18.7 shows the five domains of criteria, with some limited

TABLE 18.7 ■ Five domains of GRADE approach to quality of evidence

Domain	As applied in this chapter	Examples of failure
Study limitations	Risk of bias	No blinding; not intention-to-treat analysis
Inconsistency of results	Heterogeneity	$I^2 \geq 50\%$
Indirectness of evidence	(a) not direct comparison (b) diversity between studies	(a) NMA (b) Atypical acupuncture technique; atypical patients
Imprecision	Lack of confidence in the mean	Small samples and wide confidence intervals
Publication bias	Not discussed here	Larger studies more likely to be negative

applications for our purposes, and examples. The method is described by [Guyatt et al. \(2008\)](#), and GRADE software semi-automates the construction of a Summary of findings table within a Cochrane Review. The GRADE method does not abolish subjectivity, but at least the decisions are transparent and can be debated and modified.

Once the evidence quality has been assessed, guideline developers can decide whether it is strong enough to recommend the treatment or not in relation to its safety and cost.

INFORMAL APPROACH TO CHECKING THE INTERPRETATION

Most readers will not need to apply the GRADE method, but may still be interested in judging whether a review’s conclusion is justified or not. Be particularly concerned if the authors have given no ‘thoughtful consideration’ to the evidence at all. One way or another, they should address four specific aspects of the evidence, albeit subjective ([Table 18.8](#)).

The interpretation section of a review should follow the stages of a conventional article ‘Discussion’ section: summarise the main results; evaluate their strengths and weaknesses (as per [Table 18.7](#)); compare with other reviews of the same studies. Finally, the reviewers should draw justifiable conclusions in the form of implications for clinical practice and for research.

TABLE 18.8 ■ Informal checklist for appraising a review’s conclusions

Aspect of evidence	Relevant questions
A Original study data	Is the evidence plentiful? What is the risk of bias? Is the ‘acupuncture’ used similar to your own?
B Results	Do forest plots show heterogeneity? Can any heterogeneity be explained by clinical diversity? Are CIs narrow? Do CIs cross the line of zero effect? Do large studies with low risk of bias support the overall result? Are the findings consistent for all outcomes?
C Applicability	Is the effect clinically relevant – large enough and sustained long enough? Are other treatments available for the condition?
D Evidence overall	Does the evidence hang together? Do any studies that had to be excluded also align with the result?

## COMPARISONS WITH OTHER REVIEWS

It can be instructive to compare other similar reviews. [Linde et al. \(2009b\)](#) found acupuncture positive for reducing the frequency of TTH in both short and long term, but [Davis et al. \(2008\)](#) was negative for short term. The difference was caused by Davis' inclusion of an additional, highly positive study that widened the CI. The study did not meet Linde's inclusion criterion of minimum 8 weeks follow up. Thus the mean effect seen in Linde was 1.56 (CI 0.10, 3.02), which in Davis became 2.93 (CI -1.64, 7.49) – a larger effect yet not positive because of the wider confidence interval.

## RECOMMENDATIONS FOR RESEARCH

Authors of systematic reviews have pored closely over many clinical trials and defined their strengths and weaknesses, so they are in a strong position to make recommendations for research. For example, [Manheimer et al. \(2010\)](#) recommended continuing treatment for the long-term follow up, using EA and non-penetrating shams, and measuring participants' preferences for and expectations of acupuncture or any control intervention.

## REVIEW'S ABSTRACT

Often the only part of the systematic review that is visible to many readers is the abstract. The care with which this is written may reflect the quality of the rest of the review.

## Concluding comments

Systematic reviews offer the best summary of evidence of the effectiveness of healthcare interventions, and understandably the methods for conducting them have become accessible, semi-standardised and widely applied. However, these methods must be applied rigorously, and acupuncture trials bring several particular difficulties for reviews that are not met in the case of other therapies. Technical aspects of the review process may be unfamiliar to readers, who therefore have difficulty assessing the value of a particular review. Suggestions on how to evaluate important aspects of reviews are relatively straightforward and presented in this chapter. Systematic reviews of acupuncture range on the one hand from thoughtful considerations of the totality of the evidence leading to useful conclusions, to on the other hand superficial, mechanistic evaluations that make little contribution to the literature. Reviews of inadequate evidence whose findings are inconclusive would be better replaced by systematic narrative reviews that contribute to understanding and advise on further research.

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## *Clinical use*

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# Acupuncture for chronic pain

S. Hayhoe

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## Introduction

Acupuncture is used more commonly to treat pain than any other symptom: predominantly low back, knee, shoulder and neck pain, as well as headache and migraine (Hopton et al., 2012). This chapter will provide evidence for the use of acupuncture in chronic pain and suggestions for effective methods of treatment. Acupuncture is now offered by many primary care partnerships, either within general practice or by referral (Thomas et al., 2001), and it gained its place early in the development of hospital pain clinics (Spoerel and Leung, 1974) so that it is now uncommon to find a pain clinic without its acupuncturist, whether that be one of the clinic doctors with a special interest, a physiotherapist, or a trained non-medical acupuncturist (Woollam and Jackson, 1998).

## ACUPUNCTURE IN THE PAIN CLINIC

The chapter is written from the experience of an acupuncture service within a pain clinic, but much of the material is relevant to treatment in primary care. The benefits, problems and solutions for integrating acupuncture in the health service are discussed in Chapter 13, but this chapter

seeks to provide evidence specifically supporting the integration of acupuncture for chronic pain as a cost effective modality within normal healthcare services, both hospital and general practice.

With funding constraints, an acupuncture pain clinic is sometimes seen as an optional extra that can be dispensed with in times of economic pressure. The best pain management services, however, regard their acupuncturist as very much part of the team, rather than just an add-on service. Discussion of patients and treatments at practice or departmental meetings should allow all members of the team to have an understanding of treatment options and success rates so that inappropriate patients are not referred for acupuncture simply because there is nowhere else for them to go. Indeed, this chapter is aimed at helping clinicians determine which patients are likely to benefit from acupuncture, and then providing pointers towards suitable methods of acupuncture treatment for individual problems.

## Evidence on acupuncture

To be medically accepted any method of treatment must demonstrate that it is safe, clinically useful, has a rational mode of action, and is cost effective (White and Kawakita, 2006).

Concerning safety, there is good evidence that acupuncture is a safe treatment, with an incidence of serious adverse events (e.g. pneumothorax) of less than 1/10 000, which is classified as very rare (see Chapter 14). This is significantly lower than that for many conventional treatments. Indeed, following publication of two major British surveys (MacPherson et al., 2001; White et al., 2001) in which no serious events were found in over 66 000 treatments, Vincent (2001) assessed acupuncture in skilled hands as 'one of the safer forms of medical intervention.' Witt et al. (2009) evaluated the safety of acupuncture in over 220 000 patients in Germany and found that the adverse effects were mainly minor: bleeding, haematoma or pain, although 2.2% suffered an adverse event requiring treatment. They concluded that 'Acupuncture provided by physicians is a relatively safe treatment' but proposed a patient information form detailing the possible risks.

Demonstrating the clinical usefulness of acupuncture to a sceptical medical profession has been a painfully slow task. This is because, although there have been many positive case histories and series, until recently relatively few randomised controlled trials (RCTs) of acceptable quality with adequate patient numbers to provide a statistically sound result had been completed, and of those that were published, most trialled traditional 'real' acupuncture against non-standard 'placebo' acupuncture, which is now thought to have physiologically similar action and is probably not a placebo at all (Lund et al., 2009; Lundeberg et al., 2011): see Chapter 17. Indeed some trials have needled points as sham or placebo that can also be traditionally used as effective for the same problem, introducing a major confounding variable (Jobst, 1995). Types of bias commonly include inadequate levels of stimulation and inappropriate assessment of outcome (Bennett et al., 2011). This has resulted in many reviewers concluding they cannot recommend acupuncture due to lack of evidence from RCTs (Johnson, 2006).

The problem of the active placebo is of particular significance in some chronic pain problems (Lundeberg and Lund, 2007a) where somatic sensitivity has increased, resulting in hyperalgesia and sometimes hyperaesthesia and allodynia, such that light needling, finger pressure or even touch can result in sensations, confirmed using functional magnetic resonance imaging (fMRI) (Gracely et al., 2002), which could be therapeutic. Also, in some pain syndromes, receptive fields in the cerebral cortex expand so that a wider topographic distribution results in pain being felt following minimal stimulation anywhere around the painful area and sometimes well outside it. All this is now being recognised, and stories that 'Placebo works in acupuncture' (Times, 2005) are being rejected due to reassessment of the results of a series of German health insurance company funded three-arm trials involving many thousands of successful acupuncture treatments

(Cummings, 2009). Individual patient data meta-analysis including almost 18 000 individual patients from high quality published RCTs (Vickers et al., 2012) showed that the use of true acupuncture points was more effective than sham points, although the difference was small suggesting that there is a general effect of acupuncture needling, not confined to specific points, that contributes to the total therapeutic effect of acupuncture in chronic pain.

**Clinical points**

Evidence of mechanisms, effectiveness, safety and cost-effectiveness are now supporting the use of acupuncture in pain clinics.

Thus, studies comparing acupuncture with sham acupuncture are likely to produce many ‘false negative’ results and are difficult to interpret. Also, they are much less relevant to clinical practice than studies comparing acupuncture with usual care, or indeed with no additional care, since patients have often already tried everything else available. In this chapter, greater weight is given to usual care comparisons as these give an indication of the sort of response that is likely to be seen in clinical practice.

Acupuncture’s mode of action is discussed in Chapter 3. In summary, there is now good evidence of acupuncture’s effects on pain processing mechanisms in both spinal cord and brain, on autonomic control, and on local blood flow, inflammation and immune mechanisms, all of which could have beneficial effects in chronic pain problems. Evidence is accumulating also to support a more recent hypothesis concerning acupuncture’s modulation of glial cell activity (Burnstock, 2009). The publication of scientifically valid evidence for the neuro-physiological actions of acupuncture has undoubtedly changed medical opinion from regarding acupuncture as a dubious form of Chinese magic to accepting it as a valuable method of treating chronic pain.

There have now been several rigorous economic evaluations (individually discussed later in this chapter) funded by the UK National Health Service (NHS) or German public health insurance using the quality adjusted life year (QALY) as the basis for cost comparison. In 2008 the UK National Institute for Health and Clinical Excellence (NICE) regarded a cost per QALY gained of £20 000 as acceptable for funding by the NHS (NICE, 2008). At about the same time the equivalent figure quoted for Germany was €50 000. The evaluations so far, shown in Table 19.1, have been well within this cost limit, some significantly better than current standard treatments (Kim et al., 2012). These have been for all the most common complaints referred to pain clinics for which acupuncture is routinely used and considered effective (Handy, 1998): low back pain, chronic neck pain, headache and osteoarthritis of hip or knee.

TABLE 19.1 ■ Cost-effectiveness of acupuncture

Condition	UK study (£/QALY)	German study (€/QALY)
Low back pain	4241	10526
Headache	9951	11657
Osteoarthritis	3855	17845
Chronic neck pain	(none done)	12649

Cost per QALY (incremental cost-effectiveness ratio) for pain.  
*Reproduced with permission from Kim, S.Y., Lee, H., Chae, Y., et al., 2012. A systematic review of cost-effectiveness analyses alongside randomised controlled trials of acupuncture. Acupunct. Med. 30(4), 273–285.*

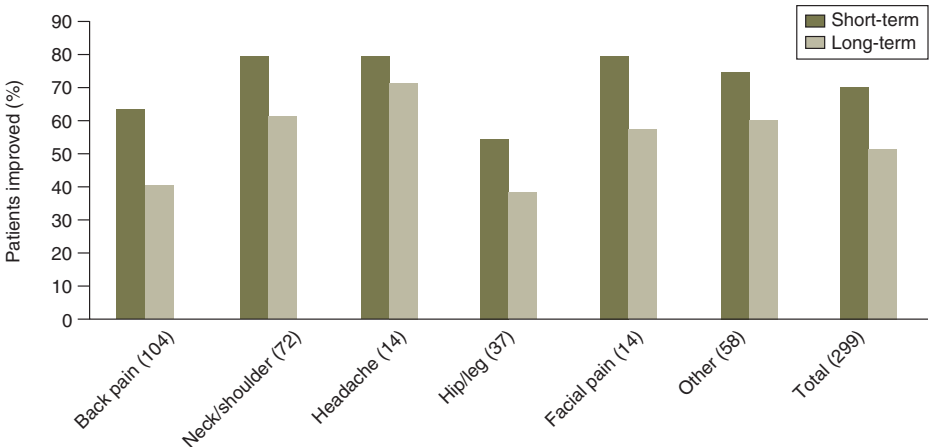
## General clinical approach using acupuncture

One of the problems with constant, oppressive pain is the variety of difficulties that it introduces to a patient's life: tension, anxiety, sometimes depression, poor response to stress, irritability, aggression, difficulty with relationships and often sleep disturbance. Acupuncture can be used to moderate all these, and all must be taken into account when assessing response to treatment.

For a number of years, audits from acupuncture clinics have reported broadly similar overall success rates with pain, with the same group of complaints obtaining the most benefit. [Spoerel and Leung \(1974\)](#) saw transient improvement in 94%, with moderate benefit in 70%. [Yamauchi \(1976\)](#) had short-term response with 83% and long-term benefit (4 months) in 43%. [Handy \(1998\)](#) found at least moderate relief in 75% while [Freedman \(2002\)](#) claimed 73%, with 61% significant improvement. Out of 5690 patients at a Spanish pain treatment unit, an audit by [Vas et al. \(2007\)](#) found that 80% had at least 50% improvement.

Transient improvement after treatment with reduction in pain, improved mobility and reduced muscle spasm, and sometimes an almost local anaesthetic-like numbness is very common (so Spoerel and Leung's 94% is quite believable) but in many cases lasts only a few hours and is thus not clinically useful. Moderate improvement lasting a few days is more acceptable and seems to be reported at around 75% in most audits. But the only relevant benefit is from the longer-term relief which occurs in about 50% of patients after a course of treatment, with the best effects being seen with headache, facial pain, and neck and shoulder pain. An audit of 234 consecutive patients (with 299 treated problems) seen over a period of 5 years in my own NHS clinic ([Fig. 19.1](#)) produced very similar results to those quoted previously with a response of 70% at end of treatment, and 51% at 1 month.

The figures from these audits show that about 25% of patients have had a good short-term response to acupuncture, but no long-term benefit. There is no straightforward solution to this problem, but some advocate adding points from a microsystem (see [Chapter 10](#)) such as auricular ([Brougham, 1992](#)), hand ([Magovern, 1995](#)) or scalp acupuncture ([Yamamoto, 1989](#)), or perhaps using distant points, or inducing analgesia through strong, painful stimulation ([Le Bars et al., 1979](#)). More likely to be of benefit is ensuring an adequate level of stimulation. Electroacupuncture, particularly combined low/high (2/100 Hz) frequencies which accelerate release of several types of endogenous opioid ([Han, 2004](#)), seems generally to be more effective than simple manual stimulation ([Tsui and Leung, 2002](#)), and high intensity stimulation ([Wang et al., 1997](#)),



**Figure 19.1** Audit of short- and long-term responses of 299 problems in 234 patients treated with acupuncture in a Pain Clinic.

sometimes even painfully strong, can be necessary for some patients. The number of needles is probably not critical beyond about five (Ceccherelli et al., 2010), provided some are placed into muscle (Vas and White, 2007), but it is suggested that the electro-stimulation needs to be applied for up to 30 min for maximal effect (Hamza et al., 1999). Concurrent medication may improve the chances of success, particularly amitriptyline which appears to have a synergistic effect with acupuncture (Fais et al., 2012), and in general it is safest not to withdraw effective drugs until improvement has proved stable.

### Clinical points

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About 50% of chronic pain patients gain long-term relief from a course of acupuncture in pain clinics.

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However, the most likely variables that influence longer-term improvement are the frequency of sessions and length of treatment course. In China, it seems that clinics often treat patients daily as an intensive course, have a short break and then repeat the course (Tsang, 1998), and some of the more successful published RCTs have given treatment twice a week (e.g. Haake et al., 2007; Molsberger et al., 2010; Tukmachi et al., 2004), but this is not always practical in a Western setting. Vas and White (2007) explored the features of the most successful RCTs (for knee osteoarthritis) compared to the least successful and found a number of differing features, one of the more important being the length of treatment course: the most successful had had at least 10 treatments. Again, unfortunately, this might not fit in with the standard system of appointments available in a routine clinic. Nonetheless it would be a pity if, for want of a few extra treatment sessions, patients were not getting the response that might have been possible with more intensive acupuncture. Self-treatment at home may be the answer for some.

### Clinical points

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Treatment courses typically consist of 6 sessions, but courses of 10 sessions are likely to have better outcomes.

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Patients who have a good, but relatively short-term response can sometimes have this response maintained by teaching a friend or relative to do simple, minimal acupuncture for them at home as required, two or three times a week if necessary (Teig et al., 2006; see also Chapter 12). Clearly the relative must be sensible enough to follow instructions and the patient must be happy to try the method (most are quite excited at the prospect!). The needles must be of a safe length and easy to handle: presterilised, disposable, half inch needles with guide tubes are suitable. After selecting one to three easy-to-access acupuncture points or trigger points that are likely to be helpful for the problem and either marking them on the skin or taking a photograph of needles in situ with the patient's mobile phone, demonstrate how to tap in a needle through its guide tube and explain that safe points that should cause no anatomical damage have been selected, so only those points may be used. Patients should be informed that adverse effects are very unlikely, but needling should not be done if the area is dirty or infected, and if there is bleeding, firm pressure with a clean tissue will stop it easily. The patients should be seen a week later to check that there are no problems, and a plastic safety box for used needles can be handed in at the clinic for proper disposal (Campbell and Hopwood, 2004). As in any other form of home treatment, the clinic doctor retains responsibility for the patient unless care has been transferred to another practitioner, so telephone access for advice must be available. This has proved a popular and safe technique which allows effective long-term management without the need for frequent clinic visits (Filshie et al., 2005; Filshie and Hester, 2006), and has the added psychological advantage that patients can feel in control of their own treatment.

Clinical points

Self acupuncture allows some patients to continue long-term pain relief.

Another possibility for longer-term regular (or as required) treatment is to run a group clinic, where eight or ten patients with similar problems can be treated at the same time. This has been successful and highly cost effective for knee osteoarthritis in a nurse-led clinic (White et al., 2012). It has proved popular with patients, who find more open access for top-up treatments is convenient and who enjoy the camaraderie of the group. However single sex groups are preferred, and the clinics are best for problems where minimal disrobing is required (Asprey et al., 2012).

Chronic pain problems

The remainder of this chapter describes individually the chronic pain problems most commonly treated with acupuncture, examining the evidence from systematic literature reviews and major trials and, where possible, noting reports of economic evaluation and the response of national funding bodies to that evidence. There is then discussion of treatment points and methods suitable for each problem – viewed from a Western medical perspective. The treatment discussed is appropriate to chronic pain patients in secondary care; patients seen in primary care, with pain for a shorter period of time, are likely to respond well to fewer needles, less stimulation, and fewer sessions.

Throughout the chapter, acupuncture points are listed in boxes for individual problems. These are intended as guides to points used in published, successful trials and case reports, and should be viewed as such, not as point prescriptions.

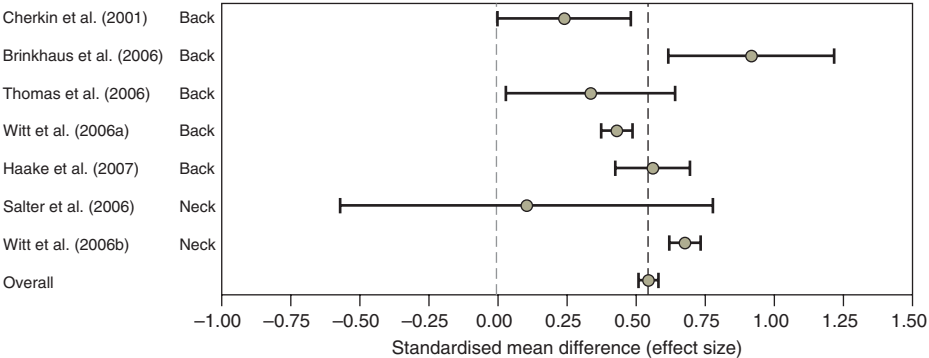
Back pain

EVIDENCE

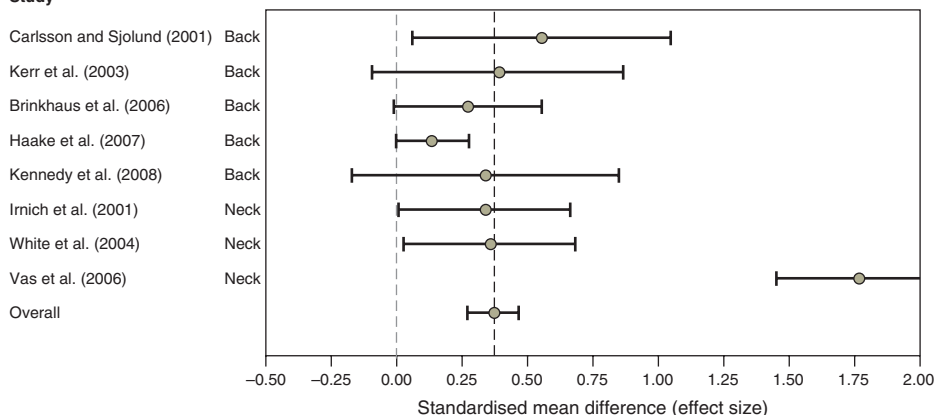
Furlan et al. (2005) reviewed 35 acupuncture trials for chronic low back pain for the Cochrane Collaboration and reported that there is evidence of pain relief and functional improvement with acupuncture, and that it improved the outcome when added to conventional therapy.

In their systematic review of individual patient data from the best quality studies, Vickers et al. (2012) analysed ‘spinal’ pain, combining studies of low back pain and neck pain. Compared with usual care in seven studies (7003 participants), acupuncture’s effect size was 0.51 (95% CI 0.36, 0.67) (see Fig. 19.2); compared with sham acupuncture in eight studies (1417 participants), the effect size was 0.26 (0.17, 0.34) (see Fig. 19.3).

Study



**Figure 19.2** Meta-analysis of high quality RCTs of acupuncture for spinal pain versus no acupuncture (Vickers et al., 2012).

**Study**

**Figure 19.3** Meta-analysis of high quality RCTs acupuncture versus sham for spinal pain (Vickers et al., 2012).

A Canadian data-analysis study (Moritz et al., 2011) reviewed 1005 patients treated with acupuncture for low back pain and found a 49% reduction in physician visits in the year following acupuncture with a consequent 37% decrease in health services cost for those who had received acupuncture compared to 2% for those having routine care.

Haake et al. (2007), in a trial supported by German public health insurance companies, included 1162 patients in their investigation and concluded that acupuncture treatment (both traditional and at sham points) was almost twice as effective as conventional therapy and gave pain relief that lasted for at least 6 months. Another German health insurance investigation (Witt et al., 2006a) involving over 11 000 patients not only reported marked clinical improvement in the acupuncture group but demonstrated a good incremental cost-effectiveness ratio of €10 526 per QALY. Following the evidence from these investigations and clinical trials the German Ministry of Health, with the advice of the Federal Committee of Physicians and Health Insurers, have approved reimbursement of acupuncture for chronic low back pain from statutory health insurance funds.

Similarly, a UK NHS-funded pragmatic trial (Thomas et al., 2006) showed benefit in the acupuncture group compared to usual care (physiotherapy, manipulation, drugs, etc.) with a statistically significant difference 2 years after treatment. Economic evaluation of this trial (Ratcliffe et al., 2006) reported a cost of £4241 per QALY gained, which equates to a modest benefit to health at relatively minor cost compared with usual care, making acupuncture cost effective in the longer term.

### Clinical points

Evidence shows that acupuncture is more effective for back pain than both no acupuncture and sham controls, and cost effective well below the recognised threshold. Guidelines recommend acupuncture for chronic back pain.

As a result of this evidence NICE in their 2009 guideline on the early management of persistent non-specific low back pain recommend offering a course of 10 sessions of acupuncture over a period of 12 weeks to patients with pain lasting more than 6 weeks (NICE [CG88], 2009). In the US, the American College of Physicians and the American Pain Society have issued joint guidelines (Chou et al., 2007) which endorse the use of acupuncture for low back pain. Lin et al. (2011) in a systematic review looking at the cost-effectiveness of guideline-endorsed treatment for low back pain found evidence for acupuncture, exercise, spinal manipulation and cognitive behavioural therapy but, interestingly, none for medication!

## CLINICAL APPROACH

Most trials that record the points used for chronic back pain rely mainly on the Bladder meridian which has over 20 points on the lower back so that needling anywhere in the area is likely to be both at the same segmental level as the pain, and on or close to a traditional acupuncture point. It is therefore more helpful to look for those that are also tender points or myofascial trigger points. These may simply be tender, may be in a taut, cord-like band of muscle that can flick under your fingers or, particularly in the low back, may be in a discrete ‘fibrositic’ nodule (Baldry, 2004; see also Chapter 7). Tender spots are often found at the dimples over the sacroiliac joints (BL27), in the area just inferior to the iliac crest and in the muscles (superficial and deep) on either side of the lumbar spinous processes (mainly BL points); indeed even if they are not tender it is often worth needling some of these points.

In addition, some practitioners like to use what has been termed ‘sacral flats’: a pair of longer needles inserted horizontally just superior to the sacral hiatus and fed in over the surface of the sacrum (BL34,33,32,31) to cover the sacral foramina on both sides (Umeh, 1986). Lumbar *Huatuojiaji* points, 0.5 cun lateral to the mid line, are also used in segmental approaches and are popularly used as local points for back pain, sometimes with periosteal tapping onto a vertebral body for additional stimulation. Electro-stimulation across appropriate needles seems to be popular with patients, providing an immediate soothing relaxation and a better and longer lasting benefit (Thomas and Lundberg, 1994).

If there is sciatic pain then the ‘sciatic’ point (BL54) in the inner, upper quadrant of the buttock is often tender and can be used together with BL60, posterior to the lateral malleolus, at the far end of the nerve. Low back problems can often give rise to pain referred into the hip area, and tender spots may be found around the hip and in a line down the lateral side of the leg (roughly following the Gall Bladder meridian) sometimes as far as GB34 below the knee. Abdominal problems may refer pain to the low back, so if there is an inadequate response with the standard approach above, it is worthwhile examining the abdomen for trigger points or tender surgical scars that can be needled (Fang, 2014).

Kalauokalani et al. (2005) compared the needling practice of physicians and non-physicians for chronic back pain and found that although the doctors based their approach on neuro-anatomic principles while the non-physicians were oriented towards Chinese tradition, there was a high correlation between the two groups for acupuncture point selection. Also, Molsberger et al. (2008), surveying experts drawn from ten countries, discovered a broad consensus in the treatment of low back pain. Points were drawn mainly from a similar preferred group of Bladder and Gall Bladder points together with *Huatuojiaji* and *Absbi* (trigger or tender) points, and practitioners all used deep needling and would vary their prescription to suit the individual patient. Essentially the needling approach as discussed earlier would be deemed appropriate.

## Neck and shoulder pain

### EVIDENCE

Neck pain and shoulder girdle pain are considered together in this section as they very often co-exist in chronic pain patients. Even patients with isolated shoulder joint pain are likely also to have neck pain; so it is of note that patients are commonly recruited to clinical trials for just one or other of these conditions, and thus may not be representative of the typical chronic pain population. The conditions are common, and fortunately the success rate with acupuncture is good: the author’s audit found a clinically useful response in 61% (Fig. 19.1).

In a systematic review and meta-analysis of 14 RCTs of acupuncture for neck pain, Fu et al. (2009) reported that acupuncture had been shown as significantly effective in the short term, but that there was insufficient evidence for conclusions as to its long-term effect. The Cochrane

review on neck disorders (Trinh et al., 2006), examining ten trials of acupuncture for chronic neck pain, concluded that patients, including those with pain radiating to the arms, had evidence of short-term pain relief following acupuncture: there was moderate evidence that acupuncture was more effective than sham (SMD  $-0.37$ , 95% CI  $-0.61$  to  $-0.12$ ). In the analysis of high quality studies by Vickers et al. (2012), the only large high quality study of acupuncture for neck pain in 3118 patients showed a highly significant effect size of 0.68 (0.63, 0.74) for acupuncture against usual care (Witt et al., 2006b). The three studies comparing acupuncture with sham reached inconsistent results (Fig. 19.3). The meta-analysis (Vickers et al., 2012) for all spinal pain is mentioned previously, under back pain.

The German health insurance investigation of acupuncture for chronic neck pain (Witt et al., 2006b) involving 14 161 patients reported that ‘Treatment with acupuncture added to routine care in patients with chronic neck pain was associated with improvements in neck pain and disability compared to treatment with routine care alone.’ Economic evaluation of this trial by Willich et al. (2006) found an incremental cost-effectiveness ratio of €12 469 per QALY gained. They concluded that ‘According to international cost-effectiveness threshold values, acupuncture is a cost effective treatment strategy in patients with chronic neck pain.’

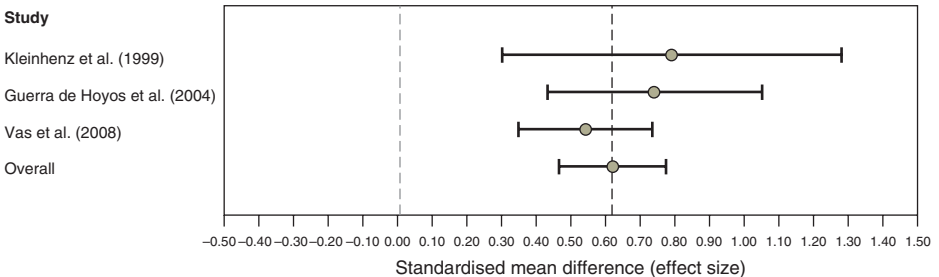
### Clinical points

Moderate evidence suggests that acupuncture is an effective treatment for neck and shoulder pain.

For shoulder pain, the Cochrane review (Green et al., 2005) found nine randomised trials. Overall, acupuncture was of benefit over placebo at 4 weeks (weighted mean difference [WMD] 17.3 (7.79, 26.81)). However, by 4 months, the difference between the acupuncture and placebo groups, whilst still statistically significant, was no longer likely to be clinically significant (WMD 3.53 (0.74, 6.32)). They concluded that there was little good evidence for the benefits of acupuncture, although short-term improvement in both pain and function is suggested. However Molsberger et al. (2010) in a major German trial with 424 participants, found a response rate of 65% in the acupuncture group, 24% in the sham group, and 37% in the group receiving conventional orthopaedic care (Fig. 19.1). They concluded that ‘acupuncture is an effective alternative to conventional orthopaedic treatment for chronic shoulder pain.’ Three studies providing individual patient data also showed significant effects against sham (Fig. 19.4).

## CLINICAL APPROACH

Chronic neck and shoulder pain (Box 19.1) often go together, with neck problems radiating down the arm, and muscular pain of the shoulder girdle affecting neck muscles and thus reducing



**Figure 19.4** Meta-analysis of high quality RCTs of acupuncture for shoulder pain versus sham acupuncture (Vickers et al., 2012).

**BOX 19.1 ■ Acupuncture points used in neck and shoulder pain trials****Neck pain**

Local: GB20, GV21, BL10, GV14, SI14, trigger points

Distant: LI4, SI3, TE5, GB34, BL60, LR3

**Shoulder pain**

SI3,9, LI11,15, TE14,15, GV14

mobility. Joint pain of the shoulder is more localised, but can still be associated with muscular involvement. So it is wise to examine both areas for primary and secondary trigger points, whatever the cause. Indeed, despite it being quite uncomfortable for the patient to have the tender points and trigger points palpated, trigger point needling is generally an effective treatment.

GB21 is almost invariably tender and is always worth using, but remember that the pleura between the first two ribs may come to within 2 cm of the surface at this point (or less in cachexic patients) so that needling should be tangential to the upper ribs to avoid a pneumothorax! GB20 and BL10 are often tender, as is BL42 in the trapezius muscle just medial to the scapula.

Palpation of the sternocleidomastoid muscle will generally elicit trigger points in the neck, and in weakly responding cases periosteal tapping on the cervical articular pillar may provide adequate stimulation for a more positive effect (Mann, 2000). Shoulder pain may be related to trigger points in the supraspinatus muscle or both anterior and posterior parts of the deltoid, but if there is little response to needling these, it is worth looking further down the arm to trigger points in the biceps muscle just above the antecubital fossa (Baldry, 2001).

As some patients find needling into the neck too painful, practitioners may omit points on the side of the neck and just use gentle electrical stimulation across needles at left and right GB21. Indeed, White et al. (2000) found that electro-stimulation of needles in posterior neck muscles produced the best results for pain relief, quality of sleep and physical activity, at least in the short term, compared to manual needling or distant electro-stimulation. Also, the number of needles seems not to be important in determining the therapeutic effect, provided at least two significant trigger points are used (Ceccherelli et al., 2010). Although Irnich et al. (2002) reported that using distant, traditional acupuncture points was more efficacious than local trigger point treatment for motion-related neck pain and for improving the range of neck movement, the very short outcome period of their trial may not have allowed for brief post-needling soreness occurring at local trigger points, so the authors still advocate trigger point use for longer-term benefit. However, I would suggest some distant points (Box 19.1), particularly arm points with a cervical nerve root such as LI4 and, where there is stress-related muscle spasm of the neck, the traditional relaxation point GV20 on the top of the head, although the perceived effect of this point may be derived from the context of care rather than the point itself (see Chapter 7).

## Headache

### EVIDENCE

Six trials published on acupuncture in headache have sample sizes greater than 200, providing solid evidence for acupuncture (Table 19.2). The response rates in the table give an indication of the expected value of acupuncture.

Vickers et al. (2004) organised an NHS-funded trial that found benefits lasting a year after treatment, with improvements that were more cost effective than standard drug treatment (Wonderling et al., 2004). The estimate of £9180 per QALY gained using acupuncture appears better than that found with sumatriptan use. However, the estimate will vary according to the

TABLE 19.2 ■ Randomised controlled trials for headache with sample size &gt;200

Reference	Diagnosis	N	Control(s)	50% Response rate		
				Acupuncture	Sham/minimal	Usual care
Vickers et al. (2004)	Chronic headache	401	Usual care	34% <sup>a</sup>	—	16% <sup>a</sup>
Linde et al. (2005)	Migraine	302	Sham; waiting list	51%	53%	15%
Melchart et al. (2005)	Tension	270	Minimal acupuncture; no acupuncture	46%	35%	4%
Diener et al. (2006)	Migraine	960/795 <sup>b</sup>	Sham; usual care	47%	33%	40%
Endres et al. (2007)	Tension	409	Sham	66%	55%	—
Jena et al. (2008)	Chronic headache	3182/2871 <sup>b</sup>	Usual care	45%	—	20%

<sup>a</sup>Value is reduction in number of days with headache.  
<sup>b</sup>Number analysed.

length of consultation and cost (salary) of the acupuncturist, although it is likely to remain within the limits of cost-effectiveness.

Large-scale trials initiated by German health insurance companies on migraine (Linde et al., 2005) and tension headache (Melchart et al., 2005) both showed semi-standardised acupuncture to be more effective than no treatment but similar to sham or minimal acupuncture. The results were seen as likely to mean that acupuncture is effective, but the positioning and stimulation level of needles are not critical.

Sun and Gan (2008) published a well conducted systematic review of 31 studies for chronic headache of both types and conclude that acupuncture is superior to sham or medication in improving headache intensity and frequency.

Two Cochrane reviews cover this area: one for migraine (Linde et al., 2009a) which reviewed 22 trials and concluded that there is consistent evidence for acupuncture in acute attacks and for prophylaxis. The review for tension headache (Linde et al., 2009b) included 11 trials and reported that acupuncture is a valuable tool for tension-type headaches. It is interesting to note that the reviews find a significant benefit of acupuncture over sham in tension headache, but not for migraine, where they suggest that 'exact point location could be of limited importance' (Linde et al., 2009a). It may be that tension headache is particularly responsive to trigger point deactivation where precise needling is essential, while migraine, being a more central phenomenon, responds to more general needling.

In their individual patient data meta-analysis of high quality RCTs Vickers et al. (2012) found an effect size of 0.42 (95% CI 0.37, 0.46) with acupuncture for chronic headache compared to no acupuncture controls. All this evidence proved persuasive in formulating the NICE guidance on headaches (NICE [CG150], 2012). They recommend a course of up to 10 sessions of acupuncture over 5–9 weeks for the prophylactic treatment of chronic tension-type headache. Similarly they suggest a course of up to ten sessions in the prophylactic treatment of migraine, with or without aura, if both topiramate and propranolol are unsuitable or ineffective.

## Clinical points

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High quality evidence shows acupuncture clearly effective for tension headache and migraine, though the effect is not point specific in migraine. Guidelines recommend acupuncture for headache.

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Some positive trials have not differentiated cluster headache from other types (Melchart et al., 2006), but clinically cluster headache has proved difficult to treat although there are rare reports of success (Gwan, 1977). Hardebo et al. (1989) found an increase in cerebro-spinal fluid (CSF) met-enkephalin after acupuncture in cluster sufferers, but noted that the treatment was of little value in preventing headaches. The problem may be due to acupuncture treatment often being aimed at what appears to be a very severe migraine-like headache, while cluster headache is in fact classed as one of the trigeminal autonomic cephalgias (Benoliel, 2012) and might show greater success with acupuncture treatment similar to that for a facial neuralgia (see 'Neuropathic pain' in a following section) (Hayhoe, 2015).

## CLINICAL APPROACH

Apart from some standard points, points can be selected according to the usual originating site of the headache and the areas it spreads to, and also to the causes or triggers of the headaches (Hayhoe, 1998), as shown in Box 19.2. This approach holds for both migraine and tension headache, but in migraine the addition of PC6 might be considered to help reduce the common nausea (Streitberger et al., 2006), and points around the eye needled superficially (BL1,2, ST1,2 and Taiyang) (Yeh et al., 2008) may help with visual symptoms.

**BOX 19.2 ■ Acupuncture points used in headache trials****Tension headache**

GB20\*,21\*, LI4\*, LR3\*

GB8,14,34, LI44, BL10,12,15, PC6,7, SP6, ST8

*Yintang, Taiyang*, neck trigger points (TPs)**Migraine**

GB14\*,20\*,40\*, BL2\*,10\*,60\*, LR3\*, LI4\*, SP6\*, ST36\*, TE5\*, GV20\*

GB2,3,8,12,21,41,42, ST8,44, CV12,13,20, GV11,15, PC6, SI3,5

*Taiyang, Yuyao, Anmian*, trigger points

\*Points marked with asterisks were reported by more than one research group.

If the patient has a headache at the time of treatment the distant points LI4 or LR3 will occasionally have a rapid effect ([Li et al., 2009](#); [Wang et al., 2012](#)), giving the patient added confidence in your expertise! One of these points plus GB20 is useful as standard.

There is some evidence that acupuncture can moderate the immune response ([Lundeberg et al., 1991](#)): various points have been suggested, but LI4 and 11 are popularly used, possibly with electro-stimulation ([Sakic et al., 1989](#)), so headache that is triggered by allergy, or food or drink sensitivity, may respond to this approach. If there is a hormonal relationship, particularly a premenstrual one, then SP6 may be useful ([Ma et al., 2010](#)). Stress, with consequent tightening of the neck and shoulder muscles, may be a trigger for both migraine and tension headaches, so a careful examination of trigger points in these muscles with needling to the most significant is suggested ([Baldry, 2001](#)), although it is worth remembering that trigger points can be secondary to the headaches rather than a cause of them. Needling can result in immediate relaxation of taut muscles with a feeling of warmth as the local blood flow improves ([Cagnie et al., 2012](#)). Causes of stress are often inherent in family or working life and cannot be eliminated, but the traditional points GV20 or *Sishencong* can in practice seem surprisingly effective in reducing the adverse responses to stress ([Lloret and Hayhoe, 2005](#)).

An occipital origin or spread of the headache suggests the use of GB20, while the other common site of origin or spread, the temple, may indicate needling at *Taiyang* after checking for trigger point pain referral from upper trapezius fibres (around GB21) or sternocleidomastoid. Nerve entrapment by the corrugator supercilii muscle has been related to recurrent migraine ([Janis et al., 2008, 2013](#)). This involves either the supraorbital or supratrochlear nerve, and needling over their respective notches at *Yuyao* or BL2 is thus appropriate for frontal headache, but inadvertent puncture of the accompanying vein or artery may result in a black eye. A rare, but potent, cause of headache can be trigger points activated in the temporalis muscle ([Simons and Travell, 1998](#)) although these are more usually secondary to postural muscle trigger points in the neck. Temporalis trigger points can also refer pain into the temporomandibular area or even into teeth. Needling can effect rapid relief.

Be warned, though, that with migraine, and to some extent tension headache, prophylactic treatment with acupuncture in sensitive subjects may induce a severe headache during the first few days after needling. However, this is likely to be the last for a good period of time, although some patients report that they still feel the warning sensations of a migraine coming on, but that it does not develop.

## Hip and knee pain

### EVIDENCE

The Cochrane review of acupuncture for peripheral joint osteoarthritis ([Manheimer et al., 2010](#)) looked at RCTs of patients with knee pain (12 trials), hip pain (3 trials) and mixed hip and knee

pain (1 trial). The review clearly highlighted the basic problem in assessing the sham-controlled trials of acupuncture: the ‘shams’ more likely to be believable to the patients were also judged to be more likely to have physiological activity, and to have clinical effects very similar to real needling. Nonetheless, they found that these trials overall showed statistically significant short-term improvement in pain and function following standard acupuncture, although the difference from sham was small. However, for trials in which acupuncture was compared to waiting list or supervised education, they reported ‘clinically relevant short- and long-term improvements in pain and function.’ The effect size compared with no acupuncture is over 0.9 (Table 19.3) which is greater than all other conservative treatments for knee osteoarthritis.

A separate Cochrane review (Casimiro et al., 2005) of acupuncture for rheumatoid arthritis found only two trials suitable for assessment, one of which had used electroacupuncture for knee pain. Although this was of poor quality and suffered from a small sample size, they reported a significant decrease in knee pain both at 24 h and at 4 months.

White and Kawakita (2006), reviewing the evidence concerning acupuncture for knee osteoarthritis, suggest that ‘On present evidence, acupuncture is likely to provide a replacement for NSAIDs, being at least equally effective, probably more cost effective, and much safer.’ A meta-analysis (Corbett et al., 2013) found acupuncture had the greatest influence on pain of all physical interventions for knee pain, when compared with usual care (Fig. 19.5).

Four, large-scale, acupuncture investigations supported by the German social health insurance companies recruited a total of 5670 patients with osteoarthritis, mainly with hip and/or knee pain (Linde et al., 2006; Scharf et al., 2006; Witt et al., 2005, 2006c). The general conclusion

TABLE 19.3 ■ Effect sizes of acupuncture for osteoarthritis, for comparison with minimally important differences – 0.39 For pain and 0.37 for function (Manheimer et al., 2010)

Outcome	N, vs. sham	N, vs. waiting list or active control
Pain, short term	8, 0.29 (0.10, 0.48)	4, 0.96 (0.70, 1.21)
Function, short term	8, 0.29 (0.08, 0.49)	3, 0.93 (0.69, 1.16)
Pain, long term	4, 0.10 (–0.01, 0.21)	3, 0.37 (0.06, 0.68) <sup>a</sup>
Function, long term	4, 0.11 (0.00, 0.22)	3, 0.36 (0.18, 0.55) <sup>a</sup>

<sup>a</sup>Figure given for combination of all available studies. N, number of included studies.

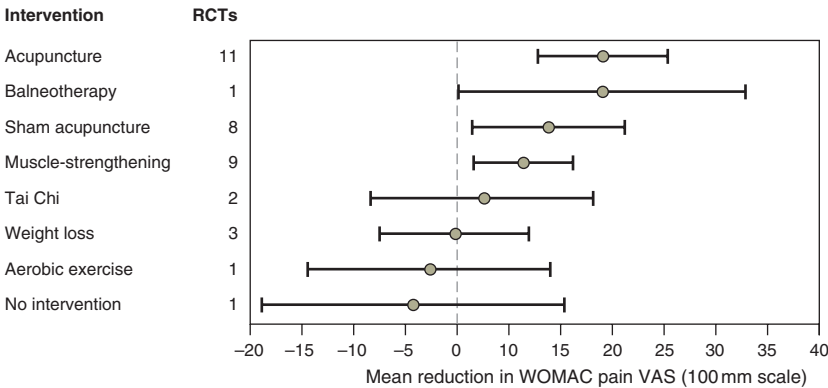


Figure 19.5 Network meta-analysis of effectiveness of physical interventions for knee pain compared with usual care (Corbett et al., 2013).

from these investigations is that acupuncture when added to routine care gives ‘marked clinical improvement’ from osteoarthritic hip and knee pain.

Reinhold et al. (2008) reported an economic analysis of the Witt et al. (2006c) trial of acupuncture for knee and hip osteoarthritis. They found that patients receiving acupuncture had an improved quality of life compared to routine care alone and that there was an overall incremental cost-effectiveness ratio of €17 845 per QALY gained, but that cost-effectiveness was better for women than for men. The conclusion was that acupuncture is a cost effective treatment for osteoarthritis pain. As a result of these trials and investigations the German Federal Committee of Physicians and Health Insurers recommended that acupuncture for osteoarthritis of the knee should be reimbursed by statutory health insurance funds, and the German Ministry of Health has now approved this.

### Clinical points

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High quality evidence confirms the effectiveness and cost-effectiveness of acupuncture for treating knee osteoarthritis. Acupuncture is recommended in guidelines.

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In the UK, the 2008 NICE guideline on osteoarthritis did not recommend acupuncture because of their assessment of its cost-effectiveness – mainly based on modelling from trials of acupuncture against sham (NICE [CG177], 2008). Since then, it has been shown that a more appropriate assessment – comparison with usual care – would have demonstrated acupuncture for knee osteoarthritis to be cost effective (Latimer et al., 2012). Subsequently, economic analysis by Whitehurst et al. (2011) of the data from an RCT of osteoarthritis of the knee by Foster et al. (2007) showed acupuncture (and sham) to be cost effective at £3889 per QALY. The Vickers meta-analysis of individual patients from high quality RCTs (Vickers et al., 2012) reported an effect size of 0.57 (95% CI 0.50, 0.64). Despite this, the revised NICE guidelines (NICE [CG177], 2014) still recommended that acupuncture should not be used. This decision was based on lack of evidence of clinical effectiveness, which NICE argued should be based on comparison with sham (since drugs are compared with placebo). NICE set the minimum clinically important difference as an effect size of 0.5 – which is not achieved by sham-controlled trials, but which is easily achieved in comparisons of acupuncture with usual care (Table 19.3).

## CLINICAL APPROACH

Vas and White (2007) analysed the studies reviewed in White et al. (2007) to identify possible factors accounting for variation in trial results. They found a number of trends giving pointers towards methods of acupuncture treatment for osteoarthritis of the knee. Their analysis showed that at least four local needles per knee, with strong electrical (rather than manual) stimulation of those in muscle, gives the best effect, but that the response is not improved by additional needling at distant points (hands or feet). Treatment should be for 20 min once a week for a minimum of 6 (preferably 10) sessions.

Audit of personal clinical experience using local points for knee pain in a pain clinic (Fig. 19.1) shows a 47% success rate – similar to the 53% achieved by the German trial of Scharf et al. (2006). Points include *Xiyan* superficially in the ‘eyes of the knee’ below the patella, *Heding* above the patella, SP10 in the vastus medialis and either ST36 or GB34 on the lateral side of the leg. These are all commonly used in positive trials (Box 19.3). However it is important to avoid needling into joints as there are reports of septic arthritis following acupuncture (Laing et al., 2002; Tien et al., 2008). Similarly, knee pain following surgery, particularly knee replacement, needs special care as needles should not be placed close to a prosthesis for fear of infection. Usually there are tender spots in the surgical scar, and these can be needled superficially along with any local muscle trigger

**BOX 19.3 ■ Acupuncture points used in trials for osteoarthritic hip and knee pain****Hip pain**

Local: GB29,30,31, BL36,37,54, ST31

Distant: GB34,43, BL60, ST40,44, LI4

**Knee pain**

GB33,34\*,39,41, BL20,40\*,57\*,58,60\*,62, ST34\*,35\*,36\*,40,44

SP4,5,6\*,9\*,10\*, KI3\*,10, LR3,8, LI4\*, TE5

*Heding\**, *Xiyan\**, trigger points\*

\*Points marked with asterisks were reported by more than one research group.

points (Fang, 2014). Nonetheless there is some evidence that strong distant points (e.g. PC6 and LR3) can be as effective as the usual local points (Liu and Tian, 2013).

Hip pain can be treated with needles to trigger points near the hip (Travell and Simons, 1992) or simply placed in a circle around the hip (surrounding the dragon) and to tender points down the side of the leg along the Gall Bladder meridian to include GB34. Generally keep to within the segmental L2 to L5 dermatomes, myotomes and sclerotomes (Box 19.3, also see Chapter 7). Bear in mind that pain around the hip may be referred from the low back, so it is certainly worth checking for trigger points in that area, and probably using some (segmental) Bladder points over the low back in addition. Clinical experience suggests that periosteal tapping onto the greater trochanter can also be of benefit (Mann, 2000).

## Neuropathic pain

### EVIDENCE

Neuralgias are notoriously difficult to treat by any means, so a relatively non-invasive technique like acupuncture seems welcome if it offers some chance of success. Liu et al. (2010) reviewed 12 RCTs of acupuncture for trigeminal neuralgia and concluded that the evidence, although of low quality, suggests that acupuncture is a useful treatment with similar benefit to carbamazepine but with fewer side effects.

Post-herpetic neuralgia, on the other hand, is a different story. There is some trial evidence (Ursini et al., 2011) that acupuncture given in acute herpes zoster is as effective an analgesic as standard drug treatment and that it might reduce the longer-term incidence of post-herpetic pain. But for post-herpetic neuralgia, although case histories and uncontrolled reports can seem enthusiastic (Lewith and Field, 1980; Valaskatgis et al., 2008), the general view is that acupuncture is not very helpful (Jolly, 1980) particularly if on chest or abdomen. Lewith et al. (1983) confirm this in their RCT, reporting that acupuncture is of little value for pain relief in postherpetic neuralgia. So clinically it is probably important to encourage treatment in the acute stage before central sensitisation has fully set, as by the time patients reach the chronic stage success is less likely.

There is some evidence that acupuncture is beneficial in peripheral neuropathy, both diabetic and HIV related (Shiflett and Schwartz, 2010; Zhang et al., 2010) and the evidence based guideline by joint American Academies on painful diabetic neuropathy recommends that 'percutaneous electric nerve stimulation should be considered' (Bril et al., 2011). In a small uncontrolled study Jeon et al. (2014) found significant improvement in pain and sensitivity after acupuncture for diabetic peripheral neuropathy with two patients gaining complete relief; also a sham-controlled RCT by Garrow et al. (2014) showed a moderate effect with acupuncture (Box 19.4 for points used in these studies).

Case histories of acupuncture for phantom limb report success for pain, but less so for phantom sensation. Treatment sessions were generally short, at around 5 min (Davies, 2013), with a

**BOX 19.4 ■ Acupuncture points used in diabetic peripheral neuropathy**

LR3\*, GB34,39,41, KI3\*, SP6\*,9,10, ST36\*, *Bafeng* (four points)

\*Points marked with asterisks were used in both studies.

**BOX 19.5 ■ Acupuncture points used for phantom limb pain****Leg amputated**

LR3, SP6, ST32,36,37

**Arm amputated**

LI4,8,11,14, GB21

small number of points (Box 19.5) on the contralateral limb (Bradbrook, 2004), but Tseng et al. (2014) successfully used only *Sishencong* on the scalp.

**CLINICAL APPROACH**

Because both allodynia and hyperalgesia occur in neuropathic pain, it can be counterproductive to needle directly into the local area, potentially causing worsening without later benefit. Instead, an appropriate technique is to place needles into the segments above and below the area and on the opposite side into the equivalent contralateral segments (Tian, 2010). The traditional advice to treat the opposite side is logical from a neuro-physiological point of view as following needling there is likely to be segmentally released neurotransmitter entering the CSF with effective spread over about three segments, as well as central neuro-hormone and transmitter release into both CSF and bloodstream, direct neural descending pain modulation which is likely to be bilateral, and glial cell modulation within the segment. Clinically, the important thing is to start with minimal stimulation and work slowly up to an effective level, including if necessary electro-stimulation, occasionally into the neuropathic area after all. This can be a slow process, needing multiple visits to achieve success, and without reducing any medication in a hurry as this can precipitate a flare-up.

In general, but particularly for the facial neuropathies, it is best not to give treatment while a neuralgia is quiescent for fear of upsetting it, so rather than giving routine follow-ups be prepared to treat as soon as symptoms recur. The neuralgia may well settle for many months, not being reactivated until triggered, for example, by a substantial mental or physical stress: this is notably true for the facial neuralgias. However then a relatively small number of acupuncture treatments will usually settle things again.

Complex regional pain syndrome (CRPS) is a similarly challenging problem with little clear evidence for the effectiveness of any form of treatment, although a multidisciplinary approach (possibly including acupuncture) seems best (Albazaz et al., 2008). There are a number of positive case histories using acupuncture, and Chan and Chow (1981) report a series of 20 patients treated with electroacupuncture showing a 70% success. The points used will vary according to the affected region, for example LI4, SI8 and HT2 have been used effectively by Leo (1983) for CRPS at the elbow, but most successful treatments seem to have used mainly local (possibly contralateral) points with electro-stimulation (Hill et al., 1991).

**Temporomandibular dysfunction**

This topic is also discussed in Chapter 38. La Touche et al. (2010a,b) reviewed eight RCTs of which four were of acceptable quality, though still at risk of bias. They found that in these trials acupuncture reduced pain, improved masticatory function and increased interincisal opening, and concluded

that ‘acupuncture is a reasonable adjunctive treatment for producing a short-term analgesic effect’ in patients with temporomandibular dysfunction (TMD). [Fink et al. \(2006\)](#) similarly reviewed eight RCTs and reported that, despite methodological shortcomings, ‘acupuncture appears to be a suitable complementary treatment method in the management of craniomandibular dysfunction.’

### Clinical points

Moderate evidence suggests acupuncture is effective for TMD.

Essentially, the clinical approach with acupuncture treatment consists of needling trigger points in the muscles acting on the joint. There are a large number of traditional acupuncture points in the area, some of which will also prove to be trigger points ([Galo et al., 2009](#)). [Rosted \(2001\)](#) analysed the points used in positive RCTs and found a consensus for ST6 and 7 and SI18, with GB20, BL10 and LI4, plus GV20 as a general relaxation point. Periosteal tapping onto the joint surface or electroacupuncture across the joint (e.g. ST6 to ST7) may prolong the benefits ([Ho and Bradley, 1992](#)) and trans-point, horizontal needling beside the ear through GB2, SI19 and TE21 provides stimulation of the facial nerve as it branches in the parotid, but beware of the proximity of the superficial temporal artery with this technique.

### Hand pain

There is little evidence for the treatment of arthritic hand pain and stiffness apart from a Cochrane review ([Brosseau et al., 2003](#)) that acupuncture-like TENS (low frequency, high intensity, transcutaneous electrical nerve stimulation) improves muscle power and decreases pain and joint tenderness in rheumatoid arthritis of the hand. Clinically, however, treatment is simple and often effective. Use the extra points known as *Baxie* which consist of a needle between each finger at the level of the knuckles, thus stimulating the territory of all the digital nerves, plus LI4, trigger points in the forearm muscles (often LI10 or 11), and tender points in the antero-lateral neck, probably related to the cervical plexus and nerve roots C6,7 and 8.

### Lateral epicondylalgia

Systematic reviews have found manual acupuncture for lateral epicondyle pain to be more effective than sham ([Gadai et al., 2014](#)) or laser ([Chang et al., 2014](#)) and a systematic review by [Trinh et al. \(2004\)](#) reported strong evidence for short-term relief. A Cochrane review also suggested short-term benefits ([Green et al., 2002](#)). Nonetheless, clinically, long-term response can be obtained by encouraging arm muscle-stretching exercises during the days following treatment ([Valera-Garrido et al., 2014](#)) and by repeating the acupuncture for at least 3 sessions. Needling the tennis elbow point at the first session in a sensitive subject can sometimes cause a flare-up of pain similar to that seen following steroid injection. A brief, gentle, periosteal peck accurately on the lateral epicondyle at the origin of the common extensor tendon (the acutely tender spot) with a very fine needle may be sufficient, but alternatively concentrate on other trigger points in the area, usually LI10 and 11, plus LI4 and tender spots in the neck, and needle the acutely tender tennis elbow spot on the second or third session, depending on response. A similar approach is appropriate for medial epicondylalgia.

### Clinical points

Moderate evidence suggests acupuncture is effective treatment for lateral epicondylitis.

## Heel pain

Heel pain is another common, apparently minor, but disabling complaint. [Cotchett et al. \(2010\)](#) conducted a systematic review of dry needling for plantar heel pain and reported the results of three trials. All showed significant success with trigger point needling or injection, but the low quality of the trials precluded firm conclusions from their results. Consensus methods of treatment ([Cotchett et al., 2011](#)) were agreed by 30 experts and involved palpating muscles, particularly those in the calf such as soleus, tibialis posterior and gastrocnemius, for trigger points ([Travell and Simons, 1992](#)) and then needling them. It would seem wise also to include some traditional acupuncture points such as BL60, LR3 and ST36 or GB34.

## Sleep disturbance

Chronic pain is a potent cause of sleep disturbance ([Ohayon, 2005](#)), but [Haack et al. \(2007\)](#) have shown that lack of sleep can, in itself, exacerbate pain through up-regulation of pro-inflammatory cytokines, producing hyperalgesic change and interfering with the response to analgesic medication ([Lautenbacher et al., 2006](#)). This vicious circle of disordered sleep and pain seriously affects quality of life during the day, so effective pain management should include strategies to improve sleep.

A Cochrane review ([Cheuk et al., 2012](#)) analysed 33 RCTs. They found that ‘acupressure resulted in more people with improvement in sleep quality’ compared to no treatment or sham, and that compared to other treatment alone, acupuncture as an adjunct ‘might marginally increase the proportion of people with improved sleep quality.’ However the effect sizes were ‘generally small with wide confidence intervals.’ A subgroup analysis suggested that manual rather than electroacupuncture was more beneficial.

Similarly, [Huang et al. \(2009\)](#) reviewing 30 studies of which 93% were positive, could not unequivocally recommend its use as they regarded few of the trials as being of adequate quality. However [Cao et al. \(2009\)](#) who were able to include many ‘fair’ quality RCTs from Chinese publications, reviewed 46 studies and concluded that ‘Acupuncture appears to be effective in treatment of insomnia.’

Patients commonly find they sleep well for a couple of nights after any acupuncture treatment, but traditional acupuncture prescriptions often include a series of points along the midline of the scalp, particularly GV20 ([Box 19.6](#)) or alternatively the group of scalp points, *Sishencong*. These supposedly have the general effects of relaxation, both mental and physical, reduction in anxiety, calming of responses and improved sleep. It may be merely a particularly strong placebo or evidence of the power of suggestion, but it does seem to be surprisingly effective even in wild animals ([Lloret and Hayhoe, 2005](#)). Clinical experience in chronic pain patients suggests that many come to specifically request it as having a calming influence on their over-stressed lives. Equally, electroacupuncture should have a similar action as it is boosting serotonin and endogenous opioid levels with consequent relaxing and euphoric effects; at the least, most patients have a good night’s sleep after treatment. For longer-term effects, patients can be taught to use HT7 acupressure at the wrist, either manually or using a commercial pressure plaster overnight ([Nordio and Romanelli, 2008](#)).

### BOX 19.6 ■ Acupuncture points used in trials for insomnia

GV20\* or *Sishencong*, HT7\*, PC6\*, KI1\*, *Anmian I\* and II\**  
 GV24, CV12,17, ST36,40, SP4,6, GB20,21,34

\*Points marked with asterisks were reported by more than one research group.

# Anxiety and depression

Chronic pain and sleep disorders are both associated with anxiety and depression (Knaster et al., 2012). These problems could be addressed during the acupuncture treatment for pain when appropriate, possibly using similar points or electro-stimulation. Errington-Evans (2012), conducting a review of acupuncture for anxiety, found a large volume of literature with consistently significant results suggesting positive effects of acupuncture, but due to poor quality methodology and the wide variety of points and treatment methods used, no firm conclusion was possible. Pilkington et al. (2007) also reported positive findings from papers included in their review, but declined to draw positive conclusions due to the poor quality of trials. Nonetheless, clinical experience suggests benefit in chronic pain patients with anxiety as a co-morbidity (for commonly used points see Box 19.7).

Similarly there is now a body of evidence suggesting clinical benefits with acupuncture for depression (MacPherson, 2014) and Han (1986) suggests that electroacupuncture, through its boosting of serotonin and noradrenaline, could be a viable alternative to antidepressants (Chapter 25). A Cochrane review (Smith et al., 2010) analysed 30 RCTs of acupuncture for depression. Many showed that manual or electroacupuncture did indeed have a similar antidepressant effect to medication, and that the combination offered additional benefit. Patients with depression as a co-morbidity seemed to gain particular help. Nonetheless, the reviewers found a generally high risk of bias and they thus reported insufficient evidence for clinical recommendation. However, analysis of a more recent pragmatic trial (MacPherson et al., 2013) by Spackman et al. (2014) found an incremental cost-effectiveness ratio of £4560 per additional QALY (probability of 0.62 for a £20000 threshold). For points used in RCTs for depression see Box 19.7. These include several which could well be used in the standard treatment of chronic pain, possibly explaining why patients often claim to feel better and happier after treatment, even if there has been no direct benefit on pain.

# Fibromyalgia

Some patients seem to have pain everywhere. After excluding polymyalgia rheumatica or some other specifically diagnosable and treatable disease, the condition could be one of the spectrum of central sensitisation syndromes, most likely fibromyalgia (Yunus, 2007). The original diagnostic criteria for fibromyalgia (Wolfe et al., 1990) specified 18 points to be palpated, of which at least 11 should be tender (Box 19.8). All are either commonly found trigger points and/or close to traditional acupuncture points (Dorsher, 2008). The revised criteria (Wolfe et al., 2010) also

BOX 19.7 ■ Acupuncture points used for anxiety and depression

Anxiety

GV20 or *Sishencong*, HT7, LI4 and 11

Depression

GV20 or *Sishencong*, *Yintang*, HT7, LI4, PC6, ST36, SP6, LR3

BOX 19.8 ■ Acupuncture points and fibromyalgia

Acupuncture points close to tender spots used in diagnosis of fibromyalgia

(American College of Rheumatology criteria: Wolfe et al., 1990)

LI11, SI12, GB20,21,30, KI25, LR8, LI17, BL48 (all bilateral)

Points used for treatment in clinical trials

LI11, SI12, GB20,21,30, KI25, LR8, various BL points

LI4, ST36, GB34, SP6, LR3, PC6, HT7

score the associated symptoms of sleep, fatigue and cognitive problems, together with a range of co-morbidities, so acupuncture treatment should be directed at these symptoms where relevant, as well as the pain (Lundeberg and Lund, 2007b).

## EVIDENCE

Langhorst et al. (2010), reviewing seven RCTs with 242 patients, found strong evidence for the short-term reduction of pain, with an effect size of 0.25 (0.02, 0.49) compared with sham acupuncture. However, they could find no evidence that acupuncture had influenced either sleep disturbance or fatigue. They could not, therefore, formally recommend acupuncture as an effective management of fibromyalgia. Nine trials (with 395 participants) were available to Deare et al. (2013) for their Cochrane review, so they were able to draw more positive conclusions. They found that electroacupuncture was better than manual in reducing pain and stiffness and improving overall well-being, sleep and fatigue, and that acupuncture probably enhances the effect of drugs and exercise on pain. They thus recommended that 'people with fibromyalgia may consider using electroacupuncture alone or with exercise and medication.'

The American NIH (1998) suggested acupuncture should be included in a comprehensive management programme of fibromyalgia. This seems a reasonable approach, as acupuncture is known to boost synthesis and release of serotonin and noradrenaline (Han, 1986), both of which are significantly reduced in fibromyalgic patients (Hayhoe, 2011a); indeed the combination of acupuncture with the drug most popular in fibromyalgia, amitriptyline (a serotonin and noradrenaline transport inhibitor), is thought to be synergistic (Fais et al., 2012).

## CLINICAL APPROACH

It is impractical to attempt to treat all the painful areas in fibromyalgia, so select the area (often neck and shoulders) that is currently causing the most intrusive pain, and treat that (Box 19.8). This can produce global benefit, but unfortunately, as these patients have marked hyperalgesia and hyperaesthesia, the initial treatment can easily cause a reactive flare-up of pain. This is usually brief, but may be sufficient to deter the patient from returning for further treatment. So needling needs to be very gentle, with as few needles as possible since each tends to cause pain on insertion. For those with neck and shoulder pain, I usually modify my standard approach to just bilateral GB21 with electroacupuncture at minimal intensity and 10Hz, which patients report to be a soothing frequency. Nonetheless, surprisingly, some patients can cope with, and need, relatively strong, deep needling (Duncan et al., 2007) thus an element of experimentation is necessary with each patient.

Apart from pain, several of the associated symptoms and co-morbidities can be responsive to acupuncture, in particular: headache and sleep disorders (see earlier in this chapter) restless legs syndrome (RLS) and irritable bowel syndrome (IBS). These are all worth treating as they can make a real difference to quality of life (Hayhoe, 2011b). The main clinical problem in doing this is that fibromyalgic patients are very sensitive, and some can bear only two or three needles, which makes it difficult to treat the co-morbidities adequately. However, as over-stimulation tends to make them worse, this has to be accepted as a limitation in some patients. A useful, validated, method of assessing response is the (revised) Fibromyalgia Impact Questionnaire (FIQ) which consists of questions relating to quality of life that measure normal activities, pain/stiffness, sleep/tiredness and anxiety/depression (Bennett et al., 2009).

## Irritable bowel syndrome

A Cochrane review of acupuncture for IBS (Manheimer et al., 2012) identified 17 RCTs and found no clear evidence of improvement compared to sham, but that acupuncture gave greater benefit than antispasmodic drugs. An earlier review by Schneider et al. (2007) recommends that this 'harmless and obviously powerful therapy' should continue in use despite its unproven effects

**BOX 19.9 ■ Acupuncture points used in trials for ibs treatment**

ST25\*,36\*, LR3\*, PC6\*

LI4, BL20,21,23, CV8,12, GV4

\*Points marked with asterisks were reported by more than one research group.

**BOX 19.10 ■ Acupuncture points used in trials for restless legs syndrome**

\*ST36, GB7,34, SP10, BL7,56,57, GV20,21, trigger points

(see also [Chapter 21](#)). There is a small selection of commonly used traditional acupuncture points ([Box 19.9](#)), but [Campbell \(1992\)](#) suggests that half a dozen needles spread over the lower abdomen with light manual stimulation can often prove helpful.

### Restless legs syndrome

The Cochrane review by [Cui et al. \(2008\)](#) found 14 trials, but only two of reasonable standard and these were of unusual design; so that although there were positive effects of acupuncture in both, the reviewers concluded that there was insufficient evidence to recommend use. A major factor in the importance of RLS in fibromyalgia is the sleep disruption that it causes ([Vignatelli et al., 2006](#)), so effective treatment could have a greater impact on quality of life than expected. Again, a small number of traditional acupuncture points have been recommended ([Box 19.10](#)), but a simple and usually beneficial approach is to needle some of the multiple trigger points to be found in the sufferer's calf muscles, in a similar manner to that described earlier for heel pain ([Cotchetti et al., 2011](#)).

### Concluding comments

The development of pain clinics has been an undoubted success story and acupuncture has played its part in that success, being particularly useful in those persistent musculo-skeletal problems that so interfere with normal life such as back, neck, hip and knee pain. Now that the treatment of pain has become a specialty in its own right, and pain management departments have changed the medical attitude towards chronic pain from one of frustrated rejection to a moderate expectation of pain relief, or at least psychological and physical improvement, acupuncture can be seen to have benefits beyond the simple analgesia looked for in the controlled trials of last century: the quality of life can show improvement in mood, sleep and activity irrespective of pain response.

Acupuncture is far from being the Chinese magic hoped for by enthusiasts, but it brings useful benefit to a substantial proportion of chronic pain patients, some of whom have had little success with any other form of treatment. A problem group of patients, consistently identified on audit, have a good response to acupuncture but for a short term only. These patients probably need more intensive treatment with longer courses, top-up treatments or possibly self-treatment at home: this is an area in need of research.

The difficulty in obtaining funding for acupuncture has been substantially due to lack of evidence of effect against 'placebo' controls. Now that large research projects have suggested that non-standard acupuncture is not a placebo, but has similar activity to more traditional forms of acupuncture, the negative findings of systematic reviews must be reassessed. This, taken with the high level of safety in skilled hands and the rigorous economic evaluation showing that acupuncture compares well (or better) with standard therapies, suggests that at least the larger

general practices should aim to have a health professional offering acupuncture treatment and that there is now no reason for any pain clinic to be without its acupuncture service.

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# Acupuncture analgesia for interventions

K. Streitberger ■ T.I. Usichenko

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## Introduction

Acupuncture has a long history in the treatment of pain. Sharp stones, so-called *Bian Shi*, might have played a role in the prehistoric time to treat painful conditions. In those times Demons were claimed to be responsible for sickness and pain, which could be eliminated by pricking holes in the body. Later needles were placed into the body, and the Demons were replaced by the theory of *Qi* and the harmony between Yin and Yang (Kaptchuk, 2002). This theory postulated that the pain conditions are caused by painful obstruction of the *Qi* flow, which could be resolved by acupuncture. The term acupuncture analgesia was later introduced within the context of performing acupuncture in anaesthesia for surgery. Initially the phenomenon of controlling pain during surgery by acupuncture was called acupuncture anaesthesia. However, as anaesthesia would include also the elimination of other sensations such as touch and temperature, this is not an accurate term. Therefore the term acupuncture anaesthesia was replaced by acupuncture assisted anaesthesia (Han, 1997) or acupuncture analgesia during surgery (Lee and Ernst, 2005). Acupuncture was also used to control postoperative and other pain conditions (Wang et al., 2008b). Whilst the treatment of chronic pain with acupuncture is described in other chapters, this chapter focuses on acute pain control during and after surgery and non-surgical interventions.

## History

The first surgery using acupuncture analgesia was reported from China in 1958 (Kho et al., 1990). This impressive introduction of acupuncture into anaesthesia was part of a political concept, elaborated by the Chinese government, to combine Traditional Chinese medical techniques and modern Western medical concepts. The first report of witnessed acupuncture analgesia during surgery was published 1971 in JAMA by Dimond (1971). Of 10 observed cases in Canton and Beijing, he described 6 in detail including surgery on the thyroid gland, abdomen, brain and lung. In all cases the patients remained awake and received only small amounts of opioids, phenobarbital or local anaesthesia. Electrical or manual stimulation was performed starting 20 min before surgery. One case was highlighted in which a thoracic surgeon was the patient undergoing lobectomy under acupuncture analgesia. He constantly quizzed the surgeon on his progress and ate an apple during a short pause in the midpoint of the hour-long operation. He was receiving acupuncture analgesia to a single needle in the left arm and appeared to have been given only 10 mg morphine sulphate preoperatively.

In discussion with the anaesthetists performing acupuncture analgesia, Dimond was told that acupuncture analgesia for surgery had been used in 4900 cases in Beijing since 1958 and in 1500 cases in Canton since 1959. Patients were usually selected only if very enthusiastic and totally accepting of the method. As Dimond commented, his report can only be understood in the context of the political reality of China. He realised that medicine and the national policy of China including ideological indoctrination were inseparable. One patient sat up after thyroid surgery, drunk a glass of milk and said 'Long live Chairman Mao and welcome American doctors' holding his little red book before leaving the operation room on foot.

Such impressive reports raised both interest and scepticism in the Western medical world. The stoicism of the Chinese, hypnosis and even deception were possible explanations. Whatever the explanation given, in 1972 Johannes Bischko in Vienna performed the first acupuncture analgesia in Europe. By stimulation of LI4 during tonsillectomy in a 38-year-old woman, he could avoid use of other anaesthetics (Benzer et al., 1972). These procedures needed intensive preoperative preparation of the patient, usually additional premedication, and could include application of local anaesthetic or intravenous analgesics during surgery on demand. Despite these early reports from the Western world, most Western scientists still were resistant to the concept of acupuncture, which appeared to be based more on oriental philosophy than on proven anatomy or physiology. Nevertheless a leading article in the journal *Lancet* (1973) discussed acupuncture analgesia in positive terms, quoting Chinese research that indicated that large-fibre stimulation and an intact nervous system appeared to be necessary for successful acupuncture analgesia. The proposal of the gate control theory of pain (Melzack and Wall, 1965), the discovery of the opioid peptides (Hughes et al., 1975) and the evidence for endogenous opioid release by acupuncture (Sjolund et al., 1977) provided a possible mechanism for acupuncture analgesia. Suddenly acupuncture analgesia appeared more credible to Western researchers, although considerable doubt about the clinical value of acupuncture has remained. It has been stated that in China the selection and preparation of patients were crucial for success and that the enthusiasm for the technique was put before concern for the patients, so they were asked to tolerate higher levels of pain (Modell et al., 1976). It was even discussed whether the Chinese race might have a higher pain tolerance (Knox et al., 1977; Johnson, 1983).

## Clinical points

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Early reports from China suggesting widespread, successful use of acupuncture alone for surgical analgesia have not been confirmed in practice; reports of its place in postoperative pain relief are more credible.

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On the other hand, Chinese physicians trained in Western medicine reported that in their hospitals during the Cultural Revolution acupuncture analgesia was performed frequently but was

later abolished because many patients cried from pain in the operating theatre (Personal communication from Wuhan Tongji Medical University Hospital).

It is now generally accepted that the original Chinese claims of an 80% success rate were over-inflated. [Murphy and Bonica \(1977\)](#) estimated that acupuncture analgesia was used in only 10% of operations in China and that, by Western standards, the response was satisfactory in only 30% of these cases. [Mann \(1974\)](#) reported an even lower satisfactory response rate of 10%. Thus, acupuncture is clearly not reliable enough on its own to be a substitute for established anaesthetic techniques. After that realisation, it was mainly promoted in combination with general anaesthesia.

Elsewhere, and especially in Europe, acupuncture analgesia combined with general anaesthesia was increasingly performed in the 1970s. After starting acupuncture stimulation, induction of anaesthesia was usually performed with a barbiturate and muscle relaxing agents. Controlled ventilation was maintained with oxygen and nitrous oxide. With this combination rapid recovery, cardiovascular stability and reduction in the need of opioid drugs was reported in heart surgery ([Herget et al., 1976](#)), as well as in thyroid surgery, abdominal surgery and eye surgery. Altogether more than 700 cases of acupuncture analgesia were reported in 1976 in the German Journal 'Anaesthetist' Volume 25 ([Doenicke et al., 1976a,b](#); [Grabow and Criveanu, 1976](#); [Herget et al., 1976](#); [Pauser et al., 1976](#)). Later, controlled studies were performed, some with promising results ([Cahn et al., 1978](#); [Kitade et al., 1990](#); [Kho et al., 1991, 1993](#)), others with less promising results ([Qin, 1996](#); [Gupta et al., 1999](#)). A systematic review on these studies came to the conclusion that the evidence was inconclusive whether acupuncture analgesia conferred any additional beneficial effect to standard anaesthetic procedures ([Lee and Ernst, 2005](#)). Nowadays, acupuncture analgesia for surgery has decreased dramatically in Europe to the state where single cases are performed by enthusiastic anaesthetists with acupuncture experience.

However, from the use of acupuncture analgesia in anaesthesia, it was reported that there might be a benefit in postoperative analgesia. Several studies were performed to demonstrate the effect of acupuncture on postoperative pain, with promising results ([Sun et al., 2008](#); [Meissner, 2009](#); [Liudden and Norheim, 2013](#)).

## Physiology

The experimental work and physiology of acupuncture analgesia is described in detail elsewhere ([Chapter 3](#)). Physiological mechanisms underlying acupuncture analgesia may be roughly divided into peripheral and central mechanisms ([Zhao, 2008](#)). A peripheral mechanism originating from muscle contraction as well as from connective tissue is postulated. Then activation of different types of afferent nerve fibres with complex interactions on pain modulation in the central nervous system plays a crucial role. Central mechanisms include a sequence of events involving complex neuronal interaction, spinal segmental mechanisms and various neuronal pathways, including brain nuclei predominantly in the limbic system ([Wang et al., 2008a](#)). Besides endogenous opioids, other transmitters and modulators involved in this integrative process at different levels of the central nervous system have been described ([Zhao, 2008](#)).

Some of those neurophysiological pathways are also commonly involved in placebo effects ([Petrovic et al., 2002](#); [Benedetti et al., 2005](#)). As one of the contributors to the placebo effect, expectancy might play an important role when acupuncture is performed in awake patients. Expectancy effects might be of importance for the size of the effect in clinical studies as shown in two independently conducted placebo-controlled trials evaluating acupuncture as an adjunctive therapy for dental surgery ([Bausell et al., 2005](#)). Participants who believed they received real acupuncture reported significantly less pain than patients who believed that they received a placebo. Expectancy effects can be almost excluded when acupuncture is performed under anaesthesia, and it does seem to be less effective than when performed before induction of anaesthesia. Placebo effects are certainly an important component of acupuncture analgesia. But according to functional imaging studies it seems that acupuncture responses in the central nervous system can be differentiated from placebo responses ([Dhond et al., 2007](#); [Harris et al., 2009](#)).

## Acupuncture points

A variety of acupuncture points have been described for acupuncture analgesia ([Tables 20.1 and 20.2](#)). For acupuncture analgesia during surgery, traditionally the acupuncture sites were chosen on the basis of ancient acupuncture charts, but also new locations were identified ([Dimond, 1971](#)). A dozen or more points were used in early operations in China, but over time there has been a trend towards fewer needles. A report from Peking Acupuncture Anaesthesia Coordinating Group ([Peking AACG, 1973](#)) describes how the number of needles used for pneumonectomy was reduced progressively from over 40 to one. Distal points are used as well as segmental points, local and paraincisional points or auricular points. Most commonly used points are LI4, PC6, ST36 and auricular points ([Chernyak and Sessler, 2005](#)).

## AURICULAR POINTS

There is wide variation in the auricular points recommended for analgesia, and indeed different systems of nomenclature are incompatible. We will describe the auricular points according to [Chapter 10](#) (Auricular acupuncture) using the WHO acupuncture nomenclature from 1987 ([WHO, 1987](#)) and give the corresponding English name according to initial Nogier classification in parentheses ([Nogier, 1977](#)). Three points that are frequently used are MA-TF1 (*Shenmen*), MA-IC1 (Lung) and MA-AH7 (Sympathetic) ([Fig. 20.1](#)) innervated by branches from the trigeminal, vagal and cervical nerves ([Peuker and Filler, 2002](#)). Points named after particular areas of the body are used as well. In a trial that showed an effect on opioid consumption in postoperative pain for hip surgery, MA-AT1 (Thalamus) was used instead of MA-AH7 (Sympathetic) in combination with MA-TF1 (*Shenmen*), MA-IC1 (Lung) and MA-AH4 (Hip) ([Usichenko et al., 2005](#)). Two studies compared the effectiveness of different auricular points. [Kitade and Hyodo \(1979\)](#) tested the level of analgesia to radiant heat at various sites of the body after stimulating various ear points. The results suggested that MA-IC1 (Lung) is the most effective point, followed by MA-AH7 (Sympathetic), MA-TF1 (*Shenmen*) and MA-SC (Kidney) in that order. MA-AH10 (Neck), and needling from MA-SF (Elbow) to MA-SF4 (Arm), produced less analgesia, and a non-acupuncture point produced no analgesia at all. [Simmons and Oleson \(1993\)](#) repeated the above-mentioned study with blinded subjects and observers. Specific points for dental pain were stimulated by a probe, and a pulp-tester was used to measure analgesia. Electroacupuncture (EA) produced an average 18% increase in the pain threshold of the intervention group, which was partially reversed by naloxone. There were no significant changes in the sham group who received stimulation at inappropriate sites.

The auricular points MA-TF1 (*Shenmen*), MA-L (Master cerebral), Tranquiliser point and Relaxation point are also described to reduce preoperative anxiety ([Chernyak and Sessler, 2005](#)).

## DISTAL POINTS

Several of the classical points are used commonly, particularly those on meridians that pass through the site of the surgery. The following points have been described as having particular attributes:

- LI4 is used for tonsillectomy, dental procedures and other surgery in the area of the head and neck region.
- LI4 and PC6 are combined for thyroidectomy and glaucoma surgery.
- ST36 and SP6 are used for lower abdominal surgery.
- a new point posterior to ST36 is called ‘appendix point’ and used for that indication.
- PC6 may be added to prevent postoperative nausea and vomiting (PONV) (see [Chapter 22](#) Nausea and vomiting).

TABLE 20.1 ■ Reports of intraoperative acupuncture analgesia

Procedure/type of anaesthesia	Reference	n	Intervention (I): stimulation/points	Control (C)	Results/comment
Abdominal minilaparotomy LA	<a href="#">Dias and Subramaniam (1984)</a>	78	EA ST26–29 long subcutaneous paraincisional needle	NC	62% without intravenous drug medication, discharged within 1 h
Abdominal surgery GA	<a href="#">Doenicke et al. (1976a,b)</a>	107	EA (10–12 Hz, 40 mA) SP4, ST36, ST25, LR13, ST18 Ear: MA-TF1, MA-IC, MA-AH	NC	Increase of HR and BP at begin of surgery; In 5% BP exceed preop values about 50%, 20 pts. had acoustic sensations, 10 pts. pain or pressure
Abdominal surgery GA	<a href="#">Kho et al. (1991)</a>	29	Combined: MA ear: MA-TF1, MA-AH6 + ES paravertebral points: BL14, BL17, BL19, BL23	NI	Stable haemodynamics, fentanyl mcg kg <sup>-1</sup> : 1.2 (I)/22.9 (C), rapid recovery; awareness: 1 (I)/2(C) No intention to treat
Abdominal surgery GA	<a href="#">Poulain et al. (1997)</a>	250	EA + TENS postoperatively HT7, SP6	NI	Fentanyl in 5% (I) compared to 100% (C) of pat., time to extubation reduced, TENS for postop pain as effective as non-narcotic analgesics
Hysterectomy GA	<a href="#">Sim et al. (2002)</a>	90	EA ST36, PC6, subcutaneously along skin incision	S (RCT)	No difference in opioid consumption ( $p=0.47$ )
Eye surgery GA	<a href="#">Abdulla et al. (1979)</a>	65	EA or ES (30 Hz, 40 mA) dermatomes of first and second trigeminal nerve, C3 and C4	Opioid	No additional analgesics, stability of circulatory system, no difference in plasma catecholamines
Heart surgery GA	<a href="#">Herget et al. (1976)</a>	131	EA (90 V, 50 Hz) TE8, TE10, ST9, ST10, SP20 Ear: MA-TF1, MA-SC, MA-IC, MA-IC1	NC (NI/historic)	BP higher, HR same, postop ventilation shorter, up to 80% less anaesthetics Control group not described
Hernia repair LA	<a href="#">Chu et al. (2003)</a>	12	EA (4 Hz) ST36, SP6, GB27–28, KI13–14, paraincisional	NC	33% satisfactory analgesia, 67% mild discomfort, requiring more LA

Continued on following page

TABLE 20.1 ■ Reports of intraoperative acupuncture analgesia (continued)

Procedure/type of anaesthesia	Reference	n	Intervention (I): stimulation/points	Control (C)	Results/comment
Low back surgery GA	<a href="#">Baum and Schilling (1979)</a>	30	EA (8–15 Hz, 30 mA), 30 min duration of stimulation in anaesthesia before surgery Ear: MA-TF1, MA-AH, MA-IC, MA-AT	NC	Stabilisation of circulatory system Analgesic effect may be due to nitrous oxide N <sub>2</sub> O
Oocyte aspiration LA	<a href="#">Stener-Victorin et al. (1999)</a>	150	EA (2 Hz) at LI4 + TE5 (2 Hz) + EA (100 Hz) at ST29 + MA at GV20, ST36	Opioid (RCT)	No difference in pain or nausea More stress and but higher implantation and pregnancy rate
Thyroidectomy GA	<a href="#">Grabow and Criveanu (1976)</a>	85	EA before induction (8–10 Hz) LI4, SP20 Ear: MA-TF1, MA-AT	NC	Acupuncture is time consuming, good analgesia
Thyroid surgery NA	<a href="#">Kho et al. (1990)</a>	20	EA at (4 Hz, up to 20 mA) Four ear points at same side: MA-AH7, MA-AH10, MA-T, MA-TF1 Additional Pethidine	NC	Mean dose of pethidine 45 mg, increased BP and respiration rate; stable HR, rapid recovery, incomplete but well tolerated analgesia
Tonsillectomy NA	<a href="#">Benzer et al. (1972)</a>	7	MA (EA in 1 patient) LI4, LU11	NC	No pain, only once additional pethidine as premedication, twice lidocaine locally

MA, manual acupuncture; ES, electrostimulation (non-invasive); EA, electroacupuncture; S, sham; GA, general anaesthesia; LA, local anaesthesia; NA, no anaesthesia; NI, no intervention; NC, no control; BP, blood pressure; HR, heart rate; RCT, randomised controlled trial.

TABLE 20.2 ■ RCTs on postoperative pain control

Condition	Reference	n	Intervention	Control	Results and comment
Abdominal surgery Epidural catheter in both groups	Kotani et al. (2001)	98	MA preoperative for up to 4 days Intradermal needles paravertebral (BL18-24 or BL20-26)	S	Good pain relief $p < 0.05^*$ Reduction of postoperative morphine and PONV, plasma catecholamines and cortisol are lower in acupuncture group
Abdominal surgery	Wang et al. (1997a)	101	ES after surgery PCA + high-ES (9–12 mA; $n = 25$ ) PCA + low-ES (4–5 mA; $n = 25$ ) LI4 and on both sides of incision	NI S	PCA-opioid requirement decreased by 65% in high-ES, 34% in low-ES and 23% in Sham High-ES > Sham*
Abdominal surgery (gyn.)	Christensen et al. (1989)	20	EA in anaesthesia after wound closure (10 and 100Hz) GV2, GV4, BL32, SP6	NI	40% less pethidine (PCA) than without EA in the first 2 h postoperatively. No difference in postoperative distress
Abdominal surgery (CCE and hysterectomy)	Grube et al. (2009)	66	MA after surgery LI4, LI11, PC6, ST36, ST44, SP6, LR3	Mm NI	Less pain, less opioid analgesics via PCA, less PONV; MA > NI*, less opioid analgesic MA > Mm*
Hysterectomy	Lin et al. (2002)	100	EA low- and high-frequency ST36	NI S	Significant lower analgesic consumption in both EA and in S, longer time for first pain medicine request in both EA
Hysterectomy	Christensen et al. (1993)	50	EA in anaesthesia before skin incision, continued to end of surgery (10 and 100Hz) GV2, GV4, BL32, SP6, ST36	NI	No significant difference in opioid requirements or metabolic distress
Hysterectomy	Sim et al. (2002)	90	EA (preop vs. postop) ST36, PC6, subcutaneously along skin incision	S RCT	Reduced postoperative analgesic consumption $p < 0.015^*$ Preop EA > postop EA
Hysterectomy	Chen et al. (1998)	100	Postoperative TENS (9–12 mA) at ST36 or local in dermatome	S	24 h postoperatively both interventions 35–39% less opioid requirements than control*
Prostatectomy	Ntritsou et al. (2014)	75	EA (100Hz) at LI4 during closure of abdominal walls and EA (4 Hz) at ST36 and LI4 immediately after extubation	S	Reduced pain and postoperative rescue analgesic consumption ( $p < 0.001$ )

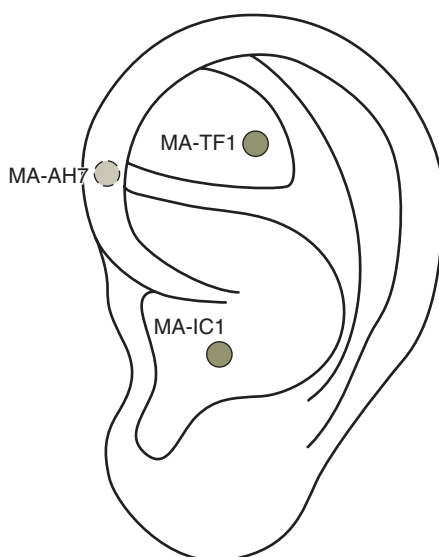
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TABLE 20.2 ■ RCTs on postoperative pain control (continued)

Condition	Reference	n	Intervention	Control	Results and comment
Hip surgery	Usichenko et al. (2005)	54	MA indwelling needle MA-TF1, MA-IC1, MA-AT1, MA-AH4	S	Reduced opioid consumption by 35%, $p=0.004^*$
Knee arthroscopy	Gupta et al. (1999)	42	MA after induction LI4, SP9, SP10, ST34, ST36	NI	Not better than without acupuncture
Knee arthroscopy	Usichenko et al. (2007)	120	MA indwelling needle MA-TF1, MA-IC1, MA-AH3	S	Reduced ibuprofen consumption by 60%; $p=0.012^*$
Oral surgery	Ekblom et al. (1991)	110	MA presurgical and postsurgical LI4, ST6, ST7, TE5, SI19	NI	Postop pain significantly increased in presurgical MA
Oral surgery	Lao et al. (1999)	39	MA LI4, ST6, ST7, TE17	S	Postoperative analgesic consumption significantly decreased*
Oral surgery	Kitade and Ohayabu (2000)	22	EA low frequency + LA Bilateral LI4 Unilateral ST6, ST7	NI	Postop pain significantly decreased
Spinal surgery	Unterrainer et al. (2010)	38	ES (TENS) pre- and postop (8h after and one day) vs. postop only Paraincisional	S	Reduced opioid consumption ES > S*, pre- and postop > postop only*

MA, manual acupuncture; ES, electrostimulation (non-invasive); EA, electroacupuncture; S, sham; GA, general anaesthesia; LA, local anaesthesia; NA, no anaesthesia; NI, no intervention; NC, no control; BP, blood pressure; HR, heart rate; RCT, randomised controlled trial; Mm, metamizol (non-opioid analgesic).

\* $p < 0.05$  or better.



**Figure 20.1** The most common auricular acupuncture points for postoperative pain.

## SEGMENTAL POINTS

Lundeberg et al. (1989) found that analgesia occurred at a lower stimulation intensity if the points were chosen from the same segment as the surgical field. Segmental points may be paravertebral points (the inner line of the bladder meridian, or *Huatuojiaji* points), or local points that have the same innervation as the organ (e.g. LI18 for thyroidectomy) or distal points in the appropriate site in the limbs. When the patient is to remain supine, flat surface electrodes may be more convenient than needles in the paravertebral region, although needles may be threaded subcutaneously and the handles bent and secured with tape. More elegant would be the insertion of 5 mm long intradermal needles, which could remain in place for up to 4 days (Kotani et al., 2001).

## LOCAL AND PARAINCISIONAL POINTS

Analgesia from distal points may not be adequate for the pain of the incision, particularly in the abdomen (Dias and Subramaniam, 1984). Long subcutaneous needles on either side of the proposed incision were described (Spoerel, 1975). Transcutaneous electrical nerve stimulation (TENS) pads or local anaesthetic infiltration are alternatives.

Local points, for example GB27, GB28, KI13 and KI14 during inguinal hernia repair, were described in combination with paraincisional needles and at the distal points ST36 and SP6 (Chu et al., 2003).

## Methods of stimulation

Different methods for stimulating acupuncture points are available, including invasive and non-invasive techniques.

Invasive stimulation is performed in the traditional manner by insertion of thin acupuncture needles which can be stimulated manually (*manual acupuncture*) or electrically (*electroacupuncture*). Stimulation without penetration of the skin by needles is defined as non-invasive stimulation.

## ELECTROACUPUNCTURE

In EA the needles are connected to an electrical stimulator. Different modes of electrostimulation can be applied which are mainly categorised into high frequency (100 Hz), medium frequency (15 Hz), and low frequency (2 Hz) stimulation (Han, 2011). High frequency stimulation is performed to provide acute short-term analgesia. It is suggested that this stimulation mode leads to release of noradrenaline serotonin and dynorphin as transmitters and is not reversible by naloxone. To achieve long-term analgesia low frequency is recommended, which releases enkephalins and endorphins, and is reversible by naloxone. Both techniques are performed with 1–40 mA according to the sensation of the patient. More detailed information can be found in Chapter 11 (Electroacupuncture).

For pain control during surgery most anaesthetists use a low frequency current for EA, at the highest intensity that the patient can bear. Usually the stimulation is started about 20 min before testing for analgesia. The intensity is adjusted as necessary to deal with accommodation, and stimulation is maintained at the same level throughout surgery. High frequency stimulation has been described at local points in combination with low frequency stimulation at distant points (Pauser et al., 1976; Stener-Victorin et al., 1999, 2003).

## MANUAL ACUPUNCTURE

In manual acupuncture (MA) stimulation of the needle may be performed by twisting up and down or rotation of the needle by hand. This stimulation should induce a complex feeling called *de qi* and described as soreness, numbness, heaviness or distension. Experienced acupuncturists may feel tightness around the needle at the same time. The release of opioids by MA is not as well documented as for EA. MA seems to release opioid peptides in different proportions compared with EA (Nappi et al., 1982) and MA appears to be less effective.

## NON-INVASIVE STIMULATION

Non-invasive stimulation is described for acute and postoperative pain and can be applied by pressure (acupressure) or by electrical stimulation via surface electrodes at the acupuncture points. Electrical stimulation is also applied to painful regions of the body, without the background of acupuncture, as TENS. TENS, administered with a strong, subnoxious intensity at a median frequency of 85 Hz in the wound area, can reduce postoperative analgesic consumption (Bjordan et al., 2003).

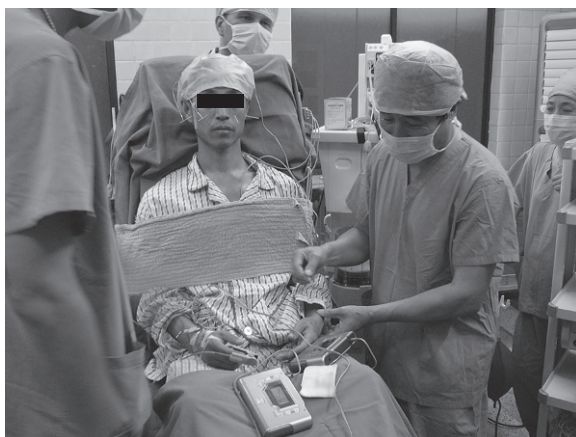
## Clinical conditions

The most spectacular clinical condition for acupuncture analgesia is pain control for surgery, especially when the patient is awake. However, control of postoperative and labour pain seem to be much more relevant clinically. Acupuncture analgesia for non-surgical interventions and postdural-puncture headaches are other interesting options.

## PAIN CONTROL DURING SURGERY

### Suitable operations

Acupuncture for controlling pain during surgery in combination with general anaesthesia was described for thyroidectomy (Kho et al., 1990), eye surgery (Abdulla et al., 1979), heart surgery (Herget et al., 1975; Hollinger et al., 1979), abdominal surgery (Doenicke et al., 1976a; Kho et al., 1991; Poulain et al., 1997), low back surgery (Baum and Schilling, 1979) and oocyte retrieval for



**Figure 20.2** Acupuncture analgesia for nasal surgery in China. (Reproduced from Streitberger, K., Shi, J., Pfab, F., Huang, W.J., Witt, C.N., Duan, Y., et al., 2010. Acupuncture assisted anesthesia for nasal surgery as an example for integrative medicine in China. *Eur. J. Integr. Med.* 2, 37–39, with permission from Elsevier.)

in vitro fertilisation (IVF) (Stener-Victorin et al., 1999; see Table 20.1). Acupuncture analgesia might be effective during short surgical procedures that are completed within 30 min and should not normally be attempted if the operation is likely to last more than 2 h.

The literature suggests that acupuncture analgesia is currently used in China mostly for head and neck surgery, such as tonsillectomy, thyroidectomy and craniotomy, and for thoracotomy. However, nowadays only a few specialised centres perform acupuncture analgesia in China in addition to local or general anaesthesia (Streitberger et al., 2010; Fig. 20.2).

### Clinical approach

For pragmatic and safety reasons acupuncture analgesia always should be performed within the modern standards of anaesthesia care including adequate monitoring and in combination with anaesthetics according to the needs of the patient.

Patients remaining conscious during the procedure must be psychologically stable and cooperative and be able to confide in the anaesthetist and surgeon. Higher educational status of the patients improves the effectiveness, and good response to suggestion and distraction are important (Parwatikar et al., 1978). Those patients should be counselled in detail about the proposed procedure. It is important to prepare them for the unusual experience that acupuncture will affect only pain, and that touch, pressure, etc. will still be felt normally. In China Qigong and other specific respiratory exercises (such as breathing with sandbags on the chest for half an hour daily!) are taught to the patients who are scheduled for thoracotomy. A trial of acupuncture analgesia may be conducted before surgery, by recording pain threshold, pain tolerance and the change of skin temperature during EA (Wong, 1993). An increase of skin temperature by 1 °C is a predictor for successful acupuncture analgesia in 80% of patients. A reduced sympathetic vasomotor activity seems to be associated with pain relief (Thomas et al., 1992).

In practice, premedication with diazepam and low-dose opioids prior to acupuncture analgesia is described (Kho et al., 1991). Needle insertion and stimulation for acupuncture analgesia for surgical procedures is usually started 20 min before induction of anaesthesia.

Standard chemical analgesics may be needed in addition and local anaesthetic may be infiltrated into the skin before incision. Conscious patients must be observed closely for any indication of pain, and intravenous analgesics should be given if necessary. In case of severe distress the anaesthetist should immediately switch to standard general anaesthesia.

If acupuncture is performed in addition to general anaesthesia, no specific patient preparation is usually necessary. Patients should be informed about the needle procedure, and if acupuncture is the only analgesic, they should be forewarned for a higher risk of awareness. The combination of acupuncture and anaesthesia was the method of choice in the West (Grabow and Criveanu, 1976, 1979; Pauser et al., 1976; Hollinger et al., 1979; Kho et al., 1991). Induction was described most commonly with a barbiturate and muscle relaxant. In modern anaesthesia usually propofol or etomidate is used as an anaesthetic induction. Controlled ventilation is usually continued with a mixture of oxygen and air or oxygen and nitrous oxide, often together with an inhalational agent.

## POSTOPERATIVE PAIN CONTROL

### Suitable operations

The reduction of postoperative pethidine requirement with EA after abdominal surgery in a controlled pilot study (Christensen et al., 1989) could not be repeated in a larger study by the same investigators (Christensen et al., 1993). In contrast, recent studies showed decreased postoperative opioid consumption after hysterectomy and other abdominal surgery by TENS (Wang et al., 1997a; Chen et al., 1998), EA (Lin et al., 2002; Sim et al., 2002; Ntritsou et al., 2014) and semi-permanent intradermal needles (Kotani et al., 2001; see Table 20.2).

Grube applied acupuncture for postoperative pain relief after laparoscopic cholecystectomy and vaginal hysterectomy recording postoperative opioid consumption via patient controlled analgesia (PCA) (Grube et al., 2009). Patients who received acupuncture reported less pain, nausea and vomiting and required less opioid analgesics than the patients from the control groups (see Table 20.2). MA after induction of anaesthesia did not reduce postoperative pain after knee arthroscopy (Gupta et al., 1999), whereas in another study with indwelling needles placed at auricular points before induction opioid consumption could be decreased (Usichenko et al., 2007). A similar application of auricular acupuncture also reduced opioid consumption after hip surgery (Usichenko et al., 2005), and TENS was effective in postoperative pain control after spinal surgery (Unterrainer et al., 2010).

### Clinical approach

Kotani et al. (2001) designed a rigorous randomised controlled trial (RCT) with an interesting acupuncture treatment concept. 175 patients scheduled for abdominal surgery were randomised into two groups, which received preoperatively an epidural catheter in combination with acupuncture or non-invasive sham acupuncture. In the acupuncture group intradermal needles were placed paravertebrally at BL18 to BL24 or BL20 to BL26, depending on the site of surgery (upper or lower abdomen). The needles stayed in place up to 4 days after surgery. Patients with acupuncture had significantly less pain, less additional morphine consumption, lower cortisol and adrenalin plasma concentrations, and less nausea and vomiting. The insertion of such a number of intradermal needles might be thought quite time consuming, but some practitioners use this method in routine practice; others prefer the other techniques described using TENS or auricular acupuncture.

For orthopaedic surgery, we suggest a simple application of auricular acupuncture, which was successfully performed in studies on knee and hip surgery (Usichenko et al., 2005, 2007). Disposable indwelling auricular needles are inserted before induction of anaesthesia at MA-TF1 (Shenmen), MA-IC1 (Lung) and the corresponding MA-AH4 (Hip) or MA-AH3 (Knee) (see Chapter 10). Also the MA-AT1 (Thalamus) could be added. The needles should be fixed with adhesive tape and retained in situ as long as the postoperative pain persists. The advantage of this method is that the patients are able to stimulate the fixed indwelling needles by themselves as soon as their pain level increases or becomes intolerable.

For abdominal surgery we suggest electrical stimulation at ST36 and paraincisional points. PC6 and LI4 could be added (Wang et al., 1997a; Chen et al., 1998; Sim et al., 2002). Stimulation

should start before surgery, but postoperative stimulation alone would also be possible. Whether stimulation is performed as TENS or as EA with needles should depend on the skills of the anaesthetist or the time available. Skilled anaesthetists could also implement the concept of Kotani with semi-permanent needles to segmental points on the back.

These simple concepts could be used with slight modifications or in combination for every other surgical intervention.

## PAIN CONTROL FOR NON-SURGICAL INTERVENTIONS

Acupuncture with electrical or manual stimulation has been used successfully for gastroscopy (Cahn *et al.*, 1978), colonoscopy (Li *et al.*, 1991; Wang *et al.*, 1997b) and extracorporeal shock-wave therapy (Chung *et al.*, 1988; Table 20.3). In colonoscopy a sham controlled study showed no significant effect of acupuncture on pain control compared to sham or no acupuncture group but less demand for sedative drugs (Fanti *et al.*, 2003). A systematic review of six RCTs concluded that the effect of acupuncture is similar to that of conventional premedication and superior to sham acupuncture for sedation before gastrointestinal endoscopy (Lee and Ernst, 2004a). As far as these diagnostic procedures are concerned, they are not associated with typical surgical tissue lesions and are not always painful, so the acupuncture might serve as a suitable alternative to premedication for these conditions.

## OBSTETRIC ANALGESIA

Both acupuncture and acupressure are effective for analgesia during labour (Smith *et al.*, 2011).

Commonly used acupuncture points for obstetric analgesia are LI4 together with SP6 (pain during contractions), GV20 (tension), LR3 (cervical rigidity), BL60 (back pain in early labour) and BL32 (back pain in late labour) (Lee and Chan, 2006).

The combination of LI4, SP6 and ST36 was described as effective in 60% for obstetric analgesia (Hyodo and Gega, 1977). LI4 and ear MA-TF1 (Shenmen) was described for one 20-min session of EA in labour to achieve good analgesia in 50% of patients, though no analgesia at all in 12.5% (Martoudis and Christofides, 1990). Besides MA-TF1 (Shenmen), the ear points MA-TF (Uterus) and MA-IC3 (Endocrine) also are commonly used in China. In individualised acupuncture approaches, a choice from the following points was provided: GV20, Yintang and LU7 as relaxing points and BL25-36, BL54, GB25-29, CV2, CV3, LI4, BL60, GB41, KI3, SP6, LR3 and subcutaneous points as analgesic points (Ramnero *et al.*, 2002). In another study, more detailed instruction for the selection of points was provided: GV20, HT7, LR3 for tension, nervousness and tiredness; LR3 and GB34 for cervical rigidity; CV4 for symphysis pain in early labour; LI10 and LI11 for pain during first stage of labour; BL23 and BL60 for back pain in early labour; BL27, BL28 and BL32 for back pain later in labour; LI4 and SP6 for strong pain during contractions; PC6 and PC7 for nausea and finally ST36 for any pain (Nesheim *et al.*, 2003).

Acupressure on SP6 for 30 min showed a decrease of labour pain for up to 60 min after pressure (Lee *et al.*, 2004). Also acupressure on LI4 and BL67 significantly reduced pain during the first stage of labour compared to sham or no treatment (Chung *et al.*, 2003).

EA seems not to be ideal in labour because of the need for needles attached to wires. TENS has been found to be more convenient.

## POSTDURAL PUNCTURE HEADACHE

Acupuncture is increasingly used in patients with severe postdural puncture headache (PDPH) (Perera, 1998; Sharma and Cheam, 2009; Dietzel *et al.*, 2013). PDPH is a severe iatrogenic complication in clinical anaesthesiology and neurology after epidural anaesthesia, spinal anaesthesia

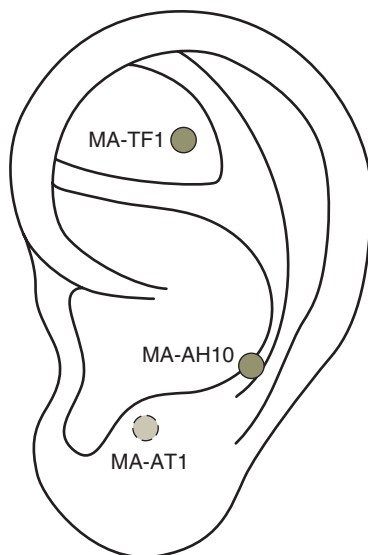
TABLE 20.3 ■ Reports of acupuncture analgesia for non-surgical interventions

Procedure anaesthesia	Reference	n	Intervention (I): stimulation/points	Control (C)	Results/comment
Colonoscopy NA	<a href="#">Fanti et al. (2003)</a>	30	EA (100Hz) LI4, SP6, SP9, ST36 Ear: MA-TF1	S	Nonsignificantly reduced pain, decreased demand for sedative*
Colonoscopy NA	<a href="#">Li et al. (1991)</a>	36	MA (4 Pat.)/EA (8 Pat.) LI4, PC6, ST36, SP5	S NI	Significant reduction of pain (VAS 1.4 (A)/2.7 (NI)/3.0 (S)) and analgesics*
Colonoscopy NA	<a href="#">Wang et al. (1997b)</a>	59	EA (2 Hz) ST36, ST37 Ear: MA-TF1	Opioid	No difference in pain
Gastroscopy NA	<a href="#">Cahn et al. (1978)</a>	90	EA (12 Hz, 1 mA) CV24, CV23, CV17, CV12, ST36, PC6, SP5	S (RCT)	Endoscopy better tolerated (less vomiting attempts, agitation) reported by nurse or endoscopist*

MA, manual acupuncture; ES, electrostimulation (non-invasive); EA, electroacupuncture; S, sham; GA, general anaesthesia; LA, local anaesthesia; NA, no anaesthesia; NI, no intervention; NC, no control; BP, blood pressure; HR, heart rate; RCT, randomised controlled trial.

\* $p < 0.05$  or better.

or lumbar puncture (Turnbull and Shepherd, 2003). PDPH has much in common with migraine in pathophysiology and clinical presentation. Both conditions are attributed to the activation of pain sensitive trigeminovascular system of the brain and subsequent reaction of intracranial vessels (Anders and Lehmann, 2013). Current empirically based drug therapies of PDPH often provide insufficient pain reduction (Basurto Ona et al., 2011). Acupuncture, described in three case series, was tried before epidural blood patch was considered and led to immediate reduction of PDPH intensity in 90% of patients, decrease or cessation of analgesics, return of the patients to normal daily activities and discharge home without further delay. The needles were inserted bilaterally (if appropriate) to a depth of 1–2 cm and left in situ for 25–30 min. Acupuncture points chosen were: BL2, BL10, BL60, BL62, GB20, LI4, LR3 and SI3, and for auricular acupuncture the needles were inserted bilaterally at points MA-TF1 (Shenmen), MA-AH10 (Neck) and MA-AT1 (Thalamus) (Fig. 20.3). We suggest that after appropriate evaluation in a randomised trial (needling as an add-on to standard therapy) acupuncture might serve as an easy to apply, low-risk therapeutic alternative in patients with severe PDPH.



**Figure 20.3** Auricular acupuncture points for postdural-puncture headache.

## Evidence

The majority of the RCTs on acupuncture analgesia are included in reviews, which are described in this chapter. Some RCTs of special interest were described in the previous sections and included in [Tables 20.1 to 20.3](#).

## ANALGESIA DURING SURGERY

In a systematic review, 19 RCTs including 1689 patients were found that compared acupuncture for analgesia during surgery with no intervention or placebo (Lee and Ernst, 2005). In the four placebo-controlled trials acupuncture was no better than the control intervention. Acupuncture was better than no intervention in 7 of 15 trials. The studies were heterogeneous concerning mode of surgery,

acupuncture therapy and outcome criteria. Moreover, it was claimed that the opioid consumption in the control group was not addressed. The authors concluded that there is no scientific support for the use of acupuncture as an adjunct to standard anaesthetic procedures during surgery. However, this statement was criticised as some appropriately performed randomised studies reporting pain relief under acupuncture during surgery (Stener-Victorin et al., 1999, 2003) were not included into the analysis, and only four placebo-controlled trials may not be enough for a sufficient analysis of efficacy (Stener-Victorin et al., 2005). Nevertheless the critics of this review did not question the common agreement that acupuncture cannot be generally recommended as an adjunct analgesic method to general anaesthesia in the intraoperative setting based on current evidence (Chernyak and Sessler, 2005; Lee and Ernst, 2005). They suggest that it might be considered as an alternative for patients desiring a non-pharmacological method or for patients who are allergic to the drugs used. This might be an option for some procedures like oocyte retrieval where it has been shown to be a viable alternative (Stener-Victorin, 2005). A subsequent study demonstrated that auricular acupuncture was able to reduce fentanyl consumption by 15% in patients during hip surgery under general anaesthesia. The difference in opioid consumption between auricular acupuncture and sham acupuncture group was statistically significant ( $4.6 \pm 1.1 \mu\text{g kg}^{-1}$  vs.  $5.2 \pm 1.3 \mu\text{g kg}^{-1}$ ; mean  $\pm$  SD;  $P=0.008$ ) but rather small to be clinically important (Wetzel et al., 2011).

Whereas some experimental investigations in animals and human volunteers found that acupuncture reduces the volatile anaesthetic requirement during general anaesthesia, the clinical investigations did not find any difference between acupuncture and control procedure. The authors of a review of acupuncture analgesia in animals reached the conclusion that EA as an adjunct to standard anaesthesia permitted a reduction of the dose of anaesthetic drugs (Janssens et al., 1988). EA for example was shown to reduce the intraoperative requirement of halothane in dogs (Tseng et al., 1981). Also in healthy volunteers who received experimental pain stimulation under general anaesthesia, auricular stimulation led to decreased desflurane concentrations (Greif et al., 2002; Taguchi et al., 2002). The reduction of anaesthetics in these 'positive' studies was quite small and seemed not to be of clinical relevance. Moreover, this effect could not be reproduced in a volunteer study where body EA was used (Morioka et al., 2002). One clinical study even showed an increased consumption of volatile anaesthetic sevoflurane in patients scheduled for laparoscopy in general anaesthesia (Kvorning et al., 2003).

## POSTOPERATIVE PAIN

Despite one study that demonstrated an increase of pain in the acupuncture group after dental surgery (Ekblom et al., 1991), a systematic review (Ernst and Pittler, 1998) suggested that acupuncture is promising in the treatment of postoperative dental pain. Those results were confirmed by two further RCTs (Lao et al., 1999; Kitade and Ohyabu, 2000).

Fifteen RCTs comparing acupuncture with sham control were included in a subsequent review on the management of postoperative pain (Sun et al., 2008). Meta-analysis of these investigations revealed that acupuncture decreased both pain intensity and opioid consumption up to 72 h after surgery. This opioid reduction effect led to a decreased incidence of opioid-related side-effects such as nausea, dizziness, sedation, pruritus and urinary retention. These results suggest that the peri-operative administration of acupuncture may be a useful adjunct for postoperative analgesia.

A meta-analysis of 21 RCTs investigating TENS for postoperative pain therapy in a total of 1350 patients showed a significant reduction of analgesic consumption with TENS (Bjoridal et al., 2003).

## Clinical points

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Good evidence supports the effect of acupuncture on postoperative pain in addition to standard pharmacologic postoperative analgesia.

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In a review of nine RCTs including only auricular acupuncture, a meta-analysis was not possible because of heterogeneity of the included studies. The evidence that auricular acupuncture reduces postoperative pain was estimated as promising but not compelling (Usichenko et al., 2008).

## OBSTETRIC ANALGESIA

In a first systematic review on acupuncture for labour pain, all three included RCTs (Lee and Ernst, 2004b) reported a significant reduction of request for meperidine and/or epidural analgesia compared to no acupuncture or sham acupuncture. Because of paucity of trial data the authors concluded that the evidence for acupuncture as an adjunct to conventional pain control during labour is promising but not convincing. A more recent Cochrane review on acupuncture or acupressure for pain management in labour with subsequent meta-analysis included 13 trials with 1986 women (Smith et al., 2011). The meta-analysis revealed reduced labour pain intensity after acupuncture versus no intervention and after acupressure versus sham control. Acupuncture was able to reduce the need for pharmacological analgesia and instrumental deliveries compared with standard care. However, a significant heterogeneity of the studies and some concerns on the quality of the trials were limitations for the interpretation of the analysis. In conclusion the authors stated ‘acupuncture and acupressure may have a role with reducing pain, increasing satisfaction with pain management and reduced use of pharmacological management’.

## Concluding comments

This selection of Western medical literature since 1970 shows the great interest of anaesthetists in acupuncture. Many reports describe the challenging and successful attempts to perform acupuncture analgesia for surgery, especially the spectacular cases, when acupuncture analgesia was performed for major surgery in awake patients. But also in combination with general anaesthesia it is still not clear whether it has a clinically relevant advantage.

One of the major benefits of acupuncture analgesia could be the reduction in need of opioid drugs which has shown to be statistically significant (Wetzel et al., 2011). However, it was of questionable clinical relevance. With reduced opioid consumption under acupuncture analgesia it has been reported that patients are more likely to be awake when they arrive in the recovery room; they are extubated earlier and suffer less PONV (Dundee et al., 1989; Ho et al., 1990; Kho et al., 1991). Even more cardiovascular stability during surgery and lack of respiratory depression after surgery was reported under acupuncture analgesia. There are in vitro reports that EA positively influences the rate of healing (Jansen et al., 1989a,b) and TENS applied to the base of the flap in women who had undergone breast surgery showed increased blood flow and survival rate (Lundeberg et al., 1988). However, these experimental results have not been verified in clinical trials yet.

Disadvantages of acupuncture analgesia during surgery are its unreliability, the increased cost in personnel time, and, in the case of EA, the inconvenience of attached wires. There is no doubt that EA does make particular demands on the staff, for example the longer induction period, and the possibility of failure of the technique. The success of the original Chinese method does depend also on excellent surgical technique and preselection of the patients. Concerning thyroid surgery in China, Kho reported that acupuncture was unable to provide total analgesia, but all patients remained quiet and calm on the operating table (Kho et al., 1990).

Despite the great interest in acupuncture analgesia in the 1970s and 1980s in Europe, especially in Germany and Austria, it has never been integrated into routine anaesthesia. Anaesthetists from those times stated that their colleagues performing acupuncture in combination with general anaesthesia used much more muscle relaxing agents instead of opioid receptor agonists. Therefore patients did not move and blood pressure usually increased (Doenicke et al., 1976a).

Besides this residual scepticism about its clinical benefit including the uncertainty of failure, the time necessary and other practical reasons have argued against its implementation to reduce or even replace intraoperative opioid consumption.

Due to inconclusive evidence, lack of clinical relevance, practical disadvantages and better modern anaesthetics, acupuncture analgesia does not play a significant role in routine clinical anaesthesia at present time. The selection of responders to acupuncture stimulation and the use of appropriate mode and appropriate strength of stimulation are important topics for future research in this area. Moreover, improved study design against the background of better understanding of underlying mechanisms of acupuncture might strengthen the future development of research in this area.

Acupuncture as an alternative to facilitate non-surgical interventions like gastroscopy and colonoscopy might be an option, but here also the evidence is not conclusive.

The evidence is strong for the use of acupuncture and related techniques in treatment of postoperative pain in addition to standard pharmacologic postoperative analgesia. Also for acupuncture analgesia during labour the evidence from RCTs is quite promising. In those conditions it might be worth evaluating its usefulness and cost effectiveness within routine performance of anaesthesia. However its integration into the clinical routine might be a long way off. The easily performed, simple and well-proven prophylaxis of PONV with stimulation at PC6 still has not been widely implemented as a routine in anaesthesia. Prof. John Dundee, who was a pioneer in the evaluation of the efficacy of PC6, in his disappointment before he died in 1991, asked his colleagues: 'I have proved that acupuncture is highly effective as a postoperative antiemetic. Why are you not using it?' (Dundee, 1991). Since then the evidence of the antiemetic effect of PC6 has increased and more positive studies have been published in high ranking journals. However, it was a long time until eventually some hospitals integrated the stimulation of PC6 into clinical pathways (Usichenko et al., 2013). It should be easy and probably beneficial for many patients to combine acupuncture for PONV and postoperative pain control.

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# Acupuncture for gastrointestinal conditions

S. Joos

## CHAPTER OUTLINE

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## Introduction

Numerous studies have been performed to investigate the effects and mechanisms of acupuncture on gastrointestinal diseases. However, compared to other areas of disease (e.g. conditions of the musculoskeletal system) the evidence in this area is rather scarce (Schneider et al., 2007).

Searching Medline for clinical studies on the efficacy of acupuncture in gastrointestinal diseases resulted in only about 200 randomised-controlled studies. Nearly half of those studies refer to the acupuncture point PC6 in nausea and vomiting. Therefore, this condition has a chapter in its own right in this textbook (Chapter 22 Nausea). The remaining studies focus on a handful of clinical conditions – mainly functional diseases – including irritable bowel syndrome (IBS), dyspepsia and oesophageal reflux. These are all common reasons for consultation in primary care. In addition, a few studies are available on inflammatory bowel diseases (IBDs) such as Crohn's disease (CD) and ulcerative colitis.

While there is an increasing number of studies showing the clinical effects of acupuncture in gastrointestinal disease, the mechanisms of action still remain unclear from the viewpoint of Western medicine. Takahashi has reviewed the available literature on mechanisms of acupuncture in the gut and summarised existing hypotheses. He concluded in his review:

*According to traditional Chinese medicine, Acupuncture is believed to restore the balance of Yin and Yang. This can be translated into the Western medicine terminology that acupuncture modulates the imbalance between the parasympathetic and sympathetic activity.*

Takahashi (2011).

More detailed, experimental studies suggest that decrease of gastric and duodenal motility is mediated by sympathetic nerves via spinal reflexes, whereas increase of motility is mediated via the vagus nerve and supraspinal reflexes (Noguchi, 2010). Niu et al. have shown in experimental studies with rabbits that cholinergic nerves, nitric oxide, motilin and stands for cholecystokinin (CCK) may contribute to mediating acupuncture effects on myoelectrical activity of the intestinal system (Niu et al., 2007). Furthermore, release of neuropeptides from nerve endings through calcitonin gene-related peptide are hypothesised to play a role in inflammatory gastrointestinal conditions (Zijlstra et al., 2003). Anti-inflammatory effects of acupuncture are also supported by the finding that alpha1-acid glycoprotein, a specific inflammation marker in IBD, significantly decreased after acupuncture in patients with active CD (Joos et al., 2004). In addition, centres in the limbic system, the hypothalamus and the brain stem are believed to play a role in modulating acupuncture effects in the treatment of gastrointestinal conditions (Noguchi, 2010).

One of the most frequently used acupuncture points to treat gastrointestinal disorders is ST36. It can be used in a wide range of gastrointestinal disorders. Another point on the stomach meridian plays an important role for treating gastrointestinal disorders: ST25. It is used especially for treating chronic colitis and diarrhoea. Furthermore, in many cases points situated on the conception vessel in the frontline of the body are used to treat gastrointestinal conditions, in particular CV6 and CV12. Other clinical approaches include a segmental approach (see Chapter 7).

Treatment approaches with acupuncture for the most common gastrointestinal disorders in primary care are described. Descriptions will include recommendations for acupuncture points in the specific condition.

## Dyspepsia and gastroparesis

Dyspepsia and gastroparesis are two common disorders of gastric motility. Dyspepsia is characterised by symptoms of postprandial fullness, epigastric pain and burning in the absence of an identifiable organic cause, whereas gastroparesis is defined as delayed gastric emptying. In many cases diabetes is the underlying cause for gastroparesis, though it can also be found postoperatively. For dyspepsia as well as for gastroparesis small pilot studies demonstrate positive effects for acupuncture. Common classical points used are ST36 and CV12.

## SYSTEMATIC REVIEW EVIDENCE

Yang et al. published a review including 14 randomised-controlled trials (RCTs) of acupuncture for relieving nonorganic dyspeptic symptoms suggestive of diabetic gastroparesis. The majority of the RCTs reported a positive effect of acupuncture in improving dyspeptic symptoms. Overall, acupuncture had a higher response rate compared to control treatments (RR, 1.20 (95% confidence interval, 1.12–1.29),  $P < 0.00001$ ) although there was no difference in solid gastric emptying between acupuncture and control. Most studies had a small sample size and high risk of bias (Yang et al., 2013).

In a study on 712 patients with dyspepsia comparing six groups with different acupuncture approaches, acupuncture on acupuncture points of the stomach meridian was most effective (Ma et al., 2012). However, another study in 68 patients showed that acupuncture treatment significantly decreased dyspepsia symptoms and improved quality of life, but there was no difference between classical points and nonspecific points (Park et al., 2009). A third study on 90 patients with dyspepsia compared acupuncture treatment, cisapride and granules containing azulene sulfonate sodium and glutamine. Symptoms, gastro-electric frequency and rhythm and gastric emptying time and plasma motilin improved significantly in the acupuncture and cisapride groups compared to the azulene group (Chen et al., 2005).

Altogether, available evidence is inadequate to conclude whether acupuncture's effect on dyspepsia might be point specific.

Evidence suggests acupuncture is effective for dyspepsia symptoms, but effects on gastric emptying time have not been demonstrated.

## Gastritis, oesophageal reflux and peptic ulcer

Gastritis, oesophageal reflux and peptic ulcer are prevalent complaints in primary care and, therefore, it is surprising that up to now research into the effects of acupuncture in these disorders is scarce. Recommended acupuncture points are LR3, LR13 and LR14 in addition to ST36 and CV12.

### EVIDENCE

A RCT comparing acupuncture plus a standard dose of omeprazole with a double dose of omeprazole in 30 adult patients with a 3-month history of symptoms related to gastro-oesophageal reflux showed that addition of acupuncture significantly decreased symptoms of daytime and night-time heartburn, acid regurgitation, dysphagia and chest pain, whereas there was no change in symptoms with double-dose omeprazole. Also, quality of life was significantly improved in the acupuncture group as compared with the double-dose omeprazole group (Dickman et al., 2007).

## Chronic constipation and flatulence

Chronic constipation, with flatulence, bloating and more extreme accumulations of gas (meteorism and tympanites) are common problems in primary care – especially in children and older adults. No specific abnormality can be identified in most of these patients, and often these problems can be explained by lifestyle factors (occupation, sedentary lifestyle, little exercise, not drinking enough, wrong nutrition, etc.).

In addition to recommendations on lifestyle, these conditions are usually treated with points on the conception vessel meridian (CV4, CV6, CV12), together with general points such as LI4 and LI11. In meteorism, a symptom sometimes accompanying constipation often presented by patients as a single symptom, ST25, ST36 can be helpful.

### EVIDENCE

There exist some studies, mainly from China, investigating the effects of acupuncture in patients with chronic constipation. The authors of a recently published meta-analysis involving 15 studies with 1052 patients concluded that acupuncture and moxibustion is effective to treat constipation. However, high-quality studies with larger sample sizes are necessary for confirming this conclusion (Du et al., 2012).

In a small pilot study acupuncture on LI11 was applied in 10 children with hospital-induced constipation before starting therapy with laxative suppositories. All participating children defaecated after a median of 3 days, and none of the children required conventional local constipation therapy (Anders et al., 2012).

## Infantile colic

Infantile colic (also known as baby colic) is defined as episodes of crying between the ages of 2 weeks and 4 months in an otherwise healthy child. The cause of the colic is generally unknown. Infantile colic can cause a major source of distress for both parents and children leading

to breastfeeding failure, postpartum depression and excess visits to the doctor. However, so far no safe and effective conventional treatment is available.

The theory has been proposed that infantile colic is a shared pathology between the mother and the baby, especially in the case of breastfeeding mothers. Tumour necrosis factor  $\alpha$  in the mother's milk and its influences on melatonin and serotonin metabolism in the baby might be major components of the pathophysiology of infantile colic (Cakmak, 2011) which can be influenced by acupuncture for the breastfeeding mother alone or also the baby.

In a prospective, quasi-randomised single blind controlled study 40 children (median 6 weeks of age) with excessive crying unresponsive to conventional therapies were treated with light needling. Children were given light needling acupuncture on one point (LI4) on both hands for 20 s on four occasions or received the same care except needling. The parents rated the light needling as more effective in improving symptoms than the control group ( $P < 0.001$ ) (Reinthal et al., 2008). The results were supported by a consecutive observational study of the same author group.

However, these findings are in contrast to a recently published study assessing acupuncture in infantile colic. In a randomised controlled multicentre trial in 13 GPs' offices needling of the acupuncture point ST36 (3 days, bilateral needling) was compared with no treatment as control in 90 patients with infantile colic. The results showed no statistically significant nor clinically relevant effect (Skjeie et al., 2013). The authors conclude that, with the current evidence, acupuncture for infantile colic should be restricted to clinical trials.

## Irritable bowel syndrome

IBS is most common among functional gastrointestinal disorders, affecting around 15% of the general population. Symptoms in IBS are very heterogeneous ranging from diarrhoea and/or constipation mostly accompanied by abdominal pain. No specific, bacterial, biochemical or morphological abnormality can be identified in these patients. Given the lack of a universally effective treatment for the diverse symptoms associated with IBS, many patients look for complementary treatment approaches.

Commonly used acupuncture points include BL18 and TE6, GB34, CV6, LR3 and SP6.

## EVIDENCE

With more than 30 clinical acupuncture studies (of which about 20 are RCTs) IBS is one of the best tested conditions in the field of gastroenterology. However, scientific evidence is conflicting. Some studies report positive effects of acupuncture on IBS symptoms (Anastasi et al., 2009; Chan et al., 1997), whereas others suggest that mostly unspecific ('placebo') effects are responsible for the improved outcomes (Lembo et al., 2009; Rohrbock et al., 2004; Schneider et al., 2006). It is known that among patients with IBS enrolled in clinical trials of conventional medical therapy, the placebo response rate is about 40% (Kaptchuk et al., 2008). Kaptchuk and colleagues have conducted some interesting and innovative studies investigating the placebo effect in IBS patients. To investigate whether placebo effects in IBS patients can experimentally be separated, they designed a study where patients received placebo, non-penetrating acupuncture alone ('limited') or placebo acupuncture with a patient-practitioner relationship augmented by warmth, attention and confidence ('augmented'). Main outcome measures were global improvement, relief of symptoms, symptom severity and quality of life. After intervention the 'augmented' group showed a significant superiority in all outcomes compared to the 'limited' group. The authors conclude that the patient-practitioner relationship is the most robust component of the 'placebo' or nonspecific effect, which is an important finding for all acupuncturists treating IBS patients. However, further analyses of the study results show that the effect attributable to different practitioners was more than twice as large as the effect attributable to treatment condition (Kelley et al., 2009).

The findings of a meta-analysis underline these findings (Manheimer et al., 2012). The authors come to the conclusion that sham-controlled RCTs have found no benefits of acupuncture relative to a credible sham acupuncture control on IBS symptom severity or IBS-related quality of life. In five comparative effectiveness Chinese trials, patients reported greater symptomatic benefits from acupuncture than from pharmacological therapies. The authors recommend future trials which should help clarify whether these reportedly greater benefits of acupuncture relative to pharmacological therapies are due entirely to patients' preferences for acupuncture or patients' greater expectations of improvement on acupuncture relative to drugs.

However, the story goes on. A recently published high-quality RCT in 233 patients, not yet been included in the abovementioned meta-analysis by Manheimer et al., found an additional benefit over usual care alone. The magnitude of the effect was sustained over the longer term; the number needed to treat was six (MacPherson et al., 2012). From an additional cost-effectiveness analysis it was concluded that acupuncture as an adjunct to usual care is not a cost-effective option for the whole IBS population but could be cost-effective for those with more severe IBS (Stamuli et al., 2012). Liver-Qi-stagnation and damp-heat were the most commonly reported patterns among the 113 patients who had received acupuncture in this study (Stuardi and MacPherson, 2012).

In an experimental study published in 2009, rats were treated with electroacupuncture at ST25 and ST37. A decrease of the number of mucosal mast cells and a downregulation in the expression of corticotropin-releasing hormone in the hypothalamus, and the expression of substance P and substance P receptor in the colon of these rats was observed (Ma et al., 2009).

Evidence suggests acupuncture is superior to no acupuncture for IBS but is conflicted whether this is greater than the effect of sham.

## Inflammatory bowel disease

IBD is a group of inflammatory conditions of the colon and small intestine. The main forms of IBD are CD and ulcerative colitis. IBD is a complex disease which is thought to arise as a result of the interaction of environmental and genetic factors followed by changes in the intestinal mucosa and dysfunction of the intestinal immune system. CD and ulcerative colitis both may present with abdominal pain, vomiting, diarrhoea, rectal bleeding, crampy abdominal pain and weight loss.

The classical points commonly used are BL20, CV12, ST36, ST25 and SP15. In addition, traditionally moxibustion is used at CV6, BL21 and SP6.

## CROHN'S DISEASE

In the authors' own randomised-controlled study in 51 patients with mild to moderately active CD, we found signs of a Spleen-Qi deficiency in all patients (Joos et al., 2004). A combination with Liver-Qi-stagnation was observed in 18 and a Kidney-Yang Deficiency in 22 of the patients. Only eight patients showed symptoms of damp-heat, and no patient had signs of cold-dampness in our study. Table 21.1 shows the acupuncture points selected according to the TCM syndromes in this study. Patients received 10 acupuncture sessions over a period of 4 weeks. In this first randomised-controlled study of acupuncture and moxibustion in active CD, a clear benefit for patients receiving acupuncture treatment compared to superficial needling at non-acupuncture points throughout the body was found (Joos et al., 2004). This design does not permit conclusions whether the effect is specific to treatment according to the principles of TCM or would occur with deep needling according to Western medical acupuncture. Disease activity significantly decreased from 250 to 163 points on the CD activity index as compared with a mean decrease from 220 to 181 in the sham group. This result remained fairly stable throughout the 12-week follow-up period. In both groups these changes were associated with improvements in general well-being

**TABLE 21.1 ■ TCM syndromes and acupuncture points used in a study of patients with Crohn's disease (Joos et al., 2004)**

Basic syndrome:	Basic acupuncture points:
Spleen-Qi deficiency	BL20, CV12, ST36, ST25 in alternation SP15
Single syndrome	+ CV6, BL21, SP6, moxa
Combined syndromes:	Additional acupuncture points:
+ Kidney-Yang-deficiency	+ CV6, BL23, GV20, GV4, moxa
+ Liver-Qi-stagnation	+ LIV3, BL18, GB34, moxa in patients with 'cold' symptoms
+ Retention of damp-heat	+ LI11, SP10, ST44

and quality of life. Furthermore, alpha1-acid glycoprotein, a specific inflammation marker for IBD, fell significantly only in the acupuncture group. Subgroup analyses revealed that higher activity grades and disease duration of less than 5 years seem to predict the efficacy of acupuncture therapy. In summary, this study suggests acupuncture as an interesting additional treatment for patients with mild to moderately active CD.

**ULCERATIVE COLITIS**

Similar to the abovementioned study in CD, the author conducted an RCT in 29 patients with ulcerative colitis (Joos et al., 2006). Underlying TCM syndromes were similar to those found in patients with CD. So, again the abovementioned five syndromes were differentiated building the basis for the selection of the following acupuncture points: BL18, BL20, BL21, BL23, CV6, CV12, GB34, GV4, GV20, LI11, LR3, ST25, ST36, ST44, SP6, SP10, SP15.

Results were similar to those of the abovementioned study on patients with CD (Joos et al., 2006). However, differences in efficacy between acupuncture and sham acupuncture were smaller in this study and significant only for the main outcome measure, which was disease activity, but not for quality of life and well-being. Reasons for this might be the lower number of patients.

In experimental studies with rats, Wu et al. observed that acupuncture markedly inhibited the expression of proinflammatory cytokines. They also found that the numbers of apoptotic cells in the colonic tissue had significantly decreased with acupuncture leading led to the conclusion that the regulation of epithelial apoptosis might be an important mechanism of acupuncture in the treatment of ulcerative colitis (Wu et al., 2004).

**Concluding comments**

Altogether, the evidence so far suggests that acupuncture has therapeutic potential for treating gastrointestinal diseases especially functional disorders. However, the evidence in the field of gastroenterology is still sparse compared to other fields of medicine and high-quality studies are urgently needed. While there are some conditions such as IBS already well investigated there are other conditions which are still 'blank spots' in acupuncture research such as gallbladder or pancreatic disorders. However, there is a great experiential knowledge about the treatment of gastrointestinal disorders by acupuncture. This needs to be preserved and to be tested within clinical studies in the future.

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# Acupuncture for nausea and vomiting

K. Streitberger

## CHAPTER OUTLINE

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## Introduction

Nausea and vomiting (NV) are common medical complaints which may occur alone or together. Vomiting or emesis is defined as oral expulsion of gastrointestinal contents as the result of contractions of the stomach and the thoracoabdominal wall musculature. Usually this action is preceded by shorter or longer period of nausea, an uncomfortable feeling of the need to vomit. Both might be associated with intoxication, various diseases or special conditions like pregnancy or sea voyages. The significance of NV ranges from a bothering, harmless episode to an acute life-saving reflex and even a chronic condition with fatal consequences like malnutrition. Therefore it is essential to treat NV within its medical context. In most cases, the treatment to relieve nausea and to prevent vomiting remains symptomatic. Dopamine antagonists and 5 HT<sub>3</sub>-(serotonin)-antagonists are effective antiemetic drugs but can be associated with adverse effects. Recently acupuncture has gained more and more interest within this context.

In a visit to China in 1983, an Irish anaesthetist named John Dundee was impressed by the use of acupressure as prophylaxis against vomiting in early pregnancy. Three years later he reported in the *British Medical Journal* that acupuncture at the acupuncture point PC6 had been used as prophylaxis for postoperative NV (PONV) in minor gynaecological operations (Dundee et al., 1986). Since then PC6 gained a reputation as being a key acupuncture point for investigating acupuncture, which lead to more than 200 randomised controlled trials cited in the medical library PubMed until now. Despite heterogeneity and some controversial results, recent meta-analyses claim an antiemetic effect of PC6 (Ezzo et al., 2005; Lee and Fan, 2009). Without doubt PC6 is the most cited acupuncture point in the context of randomised controlled trials (RCTs). However, there are other acupuncture points or point combinations which are reported to be effective for NV (Streitberger et al., 2006).

## Physiology

NV can be induced by different physiological and pathological changes, as well as drugs or ingested toxins. Within the Western scientific physiological context the vomiting centre controls NV. This centre, an area in the brainstem in the dorso-lateral reticular formation of the medulla, integrates responses and initiates the vomiting reflex. It is influenced by afferent stimuli from the cerebral cortex, cerebellar and vestibular nuclei and the chemoreceptor trigger zone (CTZ), which is comprised of a group of cells close to the area postrema on the floor of the fourth ventricle. The CTZ is very sensitive to stimuli from gastrointestinal pressure- and chemo-receptors, and to circulating chemical emetic drugs like opioids or chemotherapeutics. Dopamine, acetylcholine, histamine, serotonin and opioid receptors are found in the CTZ (Andrews, 1992; Miller, 1999; Watcha and White, 1992).

Several mechanisms of action have been proposed for the effect of acupuncture on NV (Streitberger et al., 2006) (Table 22.1). One proposed mechanism is through direct influence on the gastrointestinal smooth muscle. Electrostimulation (ES) of the acupuncture point PC6 has reduced gastric tachyarrhythmia in induced motion sickness studies (Hu et al., 1995; Stern et al., 2001) and enhanced the percentage of regular slow waves seen by electrogastrography (EGG) (Lin et al., 1997). Electroacupuncture (EA) at the acupuncture points PC6 and ST36 simultaneously decreased period dominant frequency in the EGG: stimulation at PC6 alone reduced period dominant power, and at ST36 alone increased period dominant power (Shiotani et al., 2004). EA at PC6 but not at control points suppressed retrograde peristaltic contractions and reduced vomiting episodes in seven conscious dogs with vasopressin-induced emesis (Tatewaki et al., 2005). Because this effect was abolished by naloxone, the authors concluded that a central opioid pathway was involved. Experimental studies have shown that acupuncture influences the endogenous opioid system (Han and Terenius, 1982) as well as serotonin transmission via activation of serotonergic and noradrenergic fibres (Mao et al., 1980; Takeshige et al., 1992). Those neurotransmitters are mainly known to be involved in pain processing but also influence NV.

A further proposed mechanism is that acupuncture works through a somatovisceral reflex. ES at PC6 has inhibited the rate of transient lower oesophageal sphincter relaxations triggered by gastric distension in healthy volunteers while sham acupuncture did not (Zou et al., 2005). In contrast to the previous study (Tatewaki et al., 2005), this effect was not inhibited by naloxone, thus suggesting a non-opioid mechanism, possibly a somatovisceral reflex (Zou et al., 2005). This has been previously demonstrated to affect gastric motility in rats (Sato et al., 1993).

Another mechanism suggests the stimulation of a somato-sympathetic reflex that induces gastric relaxation. In this pathway, the ventrolateral medulla neurons may play an important role (Tada et al., 2003).

According to another theory, acupuncture may influence the cerebellar vestibular neuromatrix. In an fMRI study, acupuncture at PC6 selectively activated the left superior frontal gyrus, anterior cingulate gyrus and dorsomedial nucleus of thalamus, whereas sham acupuncture or tactile stimulation did not (Yoo et al., 2004).

Many studies showed an influence of acupuncture on vagal modulation. Normalised high-frequency power of heart rate variability analysis can be used as the measure of vagal modulation. Acupuncture at PC6 but not sham acupuncture increased normalised high-frequency power, thus, suggesting vagal modulation through PC6 (Huang et al., 2005). Similar results were observed for acupuncture at PC6 in combination with the acupuncture point LI4 compared to a sham procedure (Li et al., 2005).

Anatomically, the auricular point known as 'stomach' is in the area of the vagal innervation of the auricle. It seems to be plausible that stimulation of this point might influence vagal control and consequently reduce nausea.

TABLE 22.1 ■ Experimental studies on acupuncture and nausea and vomiting

Reference	Participants	Treatment	Measurement	Results
Zou et al. (2005)	14 healthy volunteers	ES at PC6 vs. S-ES	Rate of transient lower oesophageal sphincter relaxations	40% reduction, not naloxone reversible No effect by S-ES
Tatewaki et al. (2005)	7 dogs (vasopressin-induced emesis)	EA at PC6, BL21, ST36	Episodes of vomiting and retrograde peristaltic contractions	Reduced, naloxone reversible by PC6 No effect by BL21 and ST36
Shiotani et al. (2004)	8 healthy volunteers	EA at PC6 and ST36 vs. S-EA	Electrogastrography: Period dominant frequency (PDF) and period dominant power (PDP)	PDF decreased by PC6 + ST36 PDP reduced by PC6 and increased by ST36 No effects by S-EA
Huang et al. (2005)	121 healthy volunteers	AP at PC6 vs. S-AP vs. no treatment	Heart rate variability	Increase in high-frequency power (vagal modulation) only by AP
Li et al. (2005)	29 male healthy volunteers	AP at PC6 and LI4 vs. superficial S-AP	Heart rate variability	Increase in high frequency and decrease in low frequency by AP
Lin et al. (1997)	9 healthy Chinese	ES	Electrogastrography: Gastric myoelectrical activity	ES significantly increased regular slow waves
Yoo et al. (2004)	12 healthy volunteers	AP at PC6 vs. S-AP vs. tactile stimulation	fMRI	Modulation of cerebellar vestibular neuromatrix only by PC6

AP, acupuncture; EA, electroacupuncture; ES, electrostimulation; S-AP, sham acupuncture.

And last but not least, the psychological effect of acupuncture treatment might have clinical relevance as NV is widely acknowledged to be influenced by psychological factors, such as behavioural interventions (Mundy et al., 2003). Within this context significant placebo effects must be addressed, as was shown recently for irritable bowel syndrome (Enck and Klosterhalfen, 2005; Schneider et al., 2005a). The treatment response seems to be related to high disease coping capacities (Schneider et al., 2005a), expectations (Vase et al., 2003), suggestibility (De Pascalis et al., 2002), cognitive aspects (Kreitler et al., 1987) and perception of bodily sensations during the acupuncture treatment (Schneider et al., 2005b). Still, the relationship between these treatment variables and placebo response remain unclear. Even when placebo and verum effects look similar in terms of clinical efficacy endpoints, the underlying physiological response might differ (Enck et al., 2010). For example, in a study on irritable bowel syndrome, significant differences between true acupuncture compared to controls (sham acupuncture without skin penetration at non-acupuncture points) were described in autonomic responses (diurnal profile of saliva cortisol and heart rate variability following a cardiac challenge) (Schneider et al., 2007b). While with acupuncture cortisol and heart rate variability were significantly correlated with treatment response, this was not the case with sham acupuncture.

## Clinical approach

### TREATMENT FOR DIFFERENT CLINICAL CONDITIONS

NV occur in different clinical conditions and must be treated in the context of the underlying disease. The differential acupuncture treatment of gastrointestinal disorders, for which the evidence from clinical studies remains scarce (Schneider et al., 2007a), is discussed in chapter 21. Most of the therapeutic acupuncture regimes in the treatment of disorders with symptoms of NV include PC6 and a few other selected acupuncture points (Ouyang and Chen, 2004) which will be described later. In most conditions treatment of NV remains symptomatic and pragmatic.

There are four clinical conditions associated with NV for which a large body of clinical acupuncture studies exist: PONV, chemotherapy-related NV (CRNV), pregnancy-related NV (PRNV) and motion-related NV (MRNV). The treatment of those conditions including acupuncture point selection and methods of stimulation are similar.

### ACUPUNCTURE POINTS

The most commonly described classical acupuncture point for nausea and vomiting is PC6. ST36 has been described as an adjunct point to PC6 in some studies (Shen et al., 2000; Somri et al., 2001; Ming et al., 2002; Reindl et al., 2005). Paravertebral points were included in a study of Kotani and colleague (2001) who applied intradermal needles on the back at points along the Bladder meridian, segmental to the operation site, with positive effects on both postoperative pain control and PONV.

Further points which are commonly used for their antiemetic effect, include CV12, ST21 and ST25. LR3 and LI4 also have been noted for their effect on NV (Mann, 1987). As first line they are important points for pain relief and reduction of anxiety. This effect may indirectly play a role in the alleviation of NV.

Despite the fact that most studies are performed with one antiemetic acupuncture point, in clinical practice treatment could, and frequently does, include stimulation of antiemetic points with other points. For example in the case of morning sickness PC6 and ST36 might be combined with SP4, which is often used in the treatment of dyspepsia and gastritis or with CV13, a local point for treating fullness in the epigastric region. Additionally, according to the context, points with effect on anxiety like HT7 or sedative points like GV20 might be added to antiemetic points.

## Auricular acupuncture

In auricular acupuncture, points can be selected for the areas they are supposed to represent (e.g. stomach, subcortex), for supposedly autonomic effect (e.g. sympathetic, *Shenmen*) or on the basis of Traditional Chinese Medicine ([Beijing College of Traditional Chinese Medicine et al., 1980](#)). One treatment formula which was superior to a non-penetrating sham control group in reducing postoperative vomiting after cholecystectomy comprised the auricular points sympathetic, *Shenmen*, stomach and occiput (see auricular chart, [Chapter 10](#)) ([Sahmeddini and Fazelzadehi, 2008](#)). In this case the needles were placed before induction of anaesthesia, and then fixed and kept in place perioperatively until 24 h after surgery. The possibility of using indwelling needles and the easy accessibility of the ear for the anaesthetist are advantages of auricular acupuncture. However, only a few studies have been performed to evaluate auricular acupuncture in PONV prevention ([Kim et al., 2003](#); [Sahmeddini and Fazelzadeh, 2008](#)).

## Korean hand acupuncture

In Korean hand acupuncture two acupuncture points have been described for their antiemetic effect in clinical studies: K-K9 on the palmar side of the ring finger and K-D2 on the dorsal side of the forefinger. Three controlled studies have shown that stimulation of Korean hand acupuncture points may have antiemetic effects comparable to PC6 in preventing PONV. Two studies compared tapes with and without acupressure discs ([Schlager et al., 2000](#); [Boehler et al., 2002](#)). In the other study application of a capsicum plaster was compared to an inactive plaster ([Kim et al., 2002](#)).

## METHODS OF STIMULATION

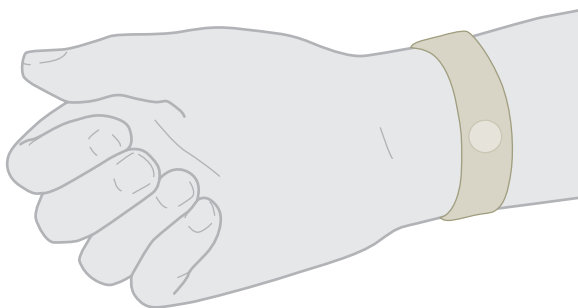
Many different methods for stimulating acupuncture points are available, including invasive and non-invasive techniques.

Invasive stimulation is performed in the traditional way of insertion of thin acupuncture needles. Needles can be stimulated manually (MA) or electrically by connecting with electrodes (EA). As a non-invasive option for children, laser stimulation at the acupuncture point PC6 showed a significant reduction of vomiting compared to sham laser in two studies. Laser stimulation was performed with wavelength of 670 nm, power 10 mW for 30 s in one study ([Schlager et al., 1998](#)) and with wavelength of 780 nm, power 20 mW for 60 s in the other one ([Butkovic et al., 2005](#)).

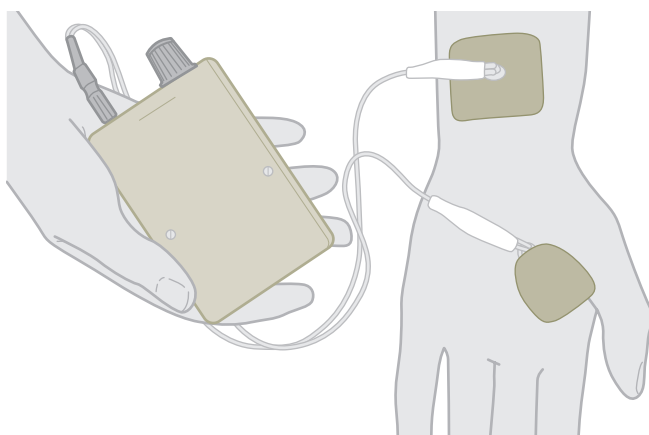
One of the most popular forms of PC6 stimulation is acupressure, for example the commercial Sea-Band® (Sea-Band Ltd, Leicestershire, England) because it is non-invasive and easy to apply. With this band a plastic button or pearl can be placed at PC6 to apply acupressure ([Fig. 22.1](#)). These bands were developed to treat seasickness by providing continuous acupressure at PC6. Acupressure can also be applied by pressing on acupuncture points with one's fingers.

A further development is the ReliefBand® (Woodside Biomedical, Inc., Abbott Park, IL, USA; Maven Laboratories, Citrus Heights, CA, USA). This band looks like a wristwatch and includes a device which applies surface electrical current at the acupuncture point. With the setting to deliver a 25 mA stimulus at 31 Hz, a significant reduction of nausea, but not vomiting, after laparoscopic surgery was reported ([Zarate et al., 2001](#)). Another form of ES is transcutaneous electrical nerve stimulation (TENS) via surface electrodes ([Fig. 22.2](#)).

A very recent development to prevent PONV was the successful use of neuromuscular monitoring devices for intraoperative PC6 stimulation ([Arnberger et al., 2007](#); [Kim et al., 2011](#)). Those devices are a tool for anaesthetists to monitor neuromuscular blockade by acceleromyography with electrical stimulation of the ulnar nerve. It has been shown that placement of the electrodes at



**Figure 22.1** Acupressure applied by Sea-Band. (*Reproduced from first edition of this book, Fig. 15.3, p. 290.*)



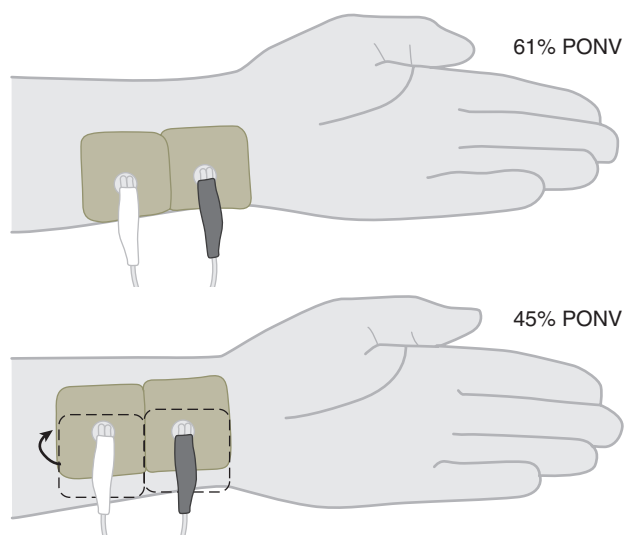
**Figure 22.2** TENS via surface electrodes. (*Reproduced from first edition of this book, Fig. 15.2, p. 298.*)

the PC6 point in the area of the median nerve and stimulation with repeated 1 Hz single twitch (Arnberger et al., 2007) or tetanic stimulation (Kim et al., 2011) significantly reduced PONV compared to stimulation at the ulnar nerve (Fig. 22.3).

There has been much debate on the optimal time to apply stimulation to prevent NV. It has been considered that PC6 stimulation prior to chemotherapy or induction of anaesthesia is most effective (Vickers, 1996). However, in more recent studies, intraoperative and postoperative stimulation have also been successful (Rusy et al., 2002; Wang and Kain, 2002; Kim et al., 2003). Stimulation prior to the exposure of emetogenic stimuli at least might have an enhanced placebo effect due to positive expectation.

## ADVERSE EFFECTS

Acupuncture performed by qualified practitioners is a relative safe therapy (Lao et al., 2003). Needling pain, hematoma, minor bleeding, orthostatic problems, forgotten needles and local skin irritation (MacPherson et al., 2001; Melchart et al., 2004; White et al., 2001) might occur as transient non-serious adverse events. Serious adverse effects like pneumothorax, cardiac tamponade, lesions of abdominal viscera and the nerve system are anecdotal and could have been avoided by careful practice and knowledge of the anatomy (Peuker et al., 1999).



**Figure 22.3** Neuromuscular monitoring device at ulnar nerve (*above*) and at PC6 (*below*) (Arnberger et al., 2007).

PC6 is located very close to the median nerve. Nevertheless, only one publication reported neuropathy of the median nerve. In this case a broken acupuncture needle was left in the carpal tunnel adjacent to PC6 (Southworth and Hartwig, 1990). Sonographic evaluations showed no nerve damage even when the nerve was punctured by an acupuncture needle (Kessler and Streitberger, 2008). However, these studies do not imply that puncturing the median nerve is safe.

In some studies discomfort, skin irritations, transient pain and swollen wrists are described after the use of acupressure bands (Lee and Done, 2004; Ezzo et al., 2005; Majholm and Møller, 2011).

## Evidence on acupuncture

More than 100 randomised controlled studies have been performed on PC6 stimulation including acupuncture in the prevention or treatment of NV. It would overextend the capacity of this chapter to describe all those trials in detail. Most of the trials are included in high quality reviews and meta-analyses, which will be described in this chapter (Table 22.2). Additionally some trials which were not included in those reviews and which are of special interest will be briefly described (Table 22.3).

## POSTOPERATIVE NAUSEA AND VOMITING

Most of the reliable scientific data exists for prevention of PONV, which is a common complaint of patients after general anaesthesia with an overall incidence of approximately 30% (Watcha and White, 1992), increasing up to 79% in high-risk patients (Apfel et al., 1999). Recommended strategies for minimising the incidence of PONV include identification of high-risk patients, avoidance of more highly emetogenic anaesthetics and multimodal therapy (Gan, 2002). Meanwhile most recommendations include non-pharmacological techniques like acupuncture, acupressure and transcutaneous nerve stimulation (Gan et al., 2003; Habib and Gan, 2004) (Fig. 22.4).

TABLE 22.2 ■ Systematic reviews on acupuncture for nausea and vomiting

Indication	Reference	Number of studies	Results (95% CI)
PONV	Vickers (1996)	33 CCT	27 pos. (11 of 12 S-Control)
		21	16 pos.
		5	5 pos.
		7	7 pos.
PONV	Lee and Done (1999)	19 RCT	Meta-analysis (compared to sham)
		5	Early N (RR 0.34 [0.20 to 0.58]) sig
		4	Late N (na)
		8	Early V (RR 0.47 [0.34 to 0.58]) sig
		5	Late V (RR 0.81 [0.46 to 1.42]) ns
	Lee and Done (2004)	26 RCT	Meta-analysis (compared to sham)
		16	N (RR 0.72 [0.59 to 0.89]) sig
		20	V (RR 0.71 [0.56 to 0.91]) sig
		15	RA (RR 0.76 [0.58 to 1.00]) sig
			Meta-analysis (compared to antiemetics)
CRNV	Ezzo et al. (2005)	5	N (RR 0.70 [0.50 to 0.98]) sig
		9	V (RR 0.92 [0.65 to 1.29]) ns
		2	RA (RR 0.78 [0.54 to 1.14]) ns
		11 RCT	Meta-analysis
		9	Acute V all (RR 0.82 [0.69 to 0.99]) sig
	Lee and Fan (2009)	4	Acute V EA+AP (RR 0.74 [0.58 to 0.94]) sig
		2	Acute V Aps (RR 0.83 [0.6 to 1.16]) ns
		4	Acute V ES (RR 0.9 [0.67 to 1.19]) ns
		7	Acute N all (SMD -0.11 [-0.25 to 0.02]) ns
		2	Acute N Aps (SMD -0.19 [-0.38 to -0.01]) sig
PONV	Lee and Fan (2009)	5	Acute N ES (SMD -0.07 [-0.23 to 0.10]) ns
		40 RCT	Meta-analysis (compared to sham)
		27	N (RR 0.71 [0.61 to 0.83]) sig
		32	V (RR 0.70 [0.59 to 0.83]) sig
		26	RA (RR 0.69 [0.57 to 0.83]) sig
			Meta-analysis (compared to antiemetics)
		9	N (RR 0.82 [0.60 to 1.13]) ns
		14	V (RR 1.01 [0.77 to 1.31]) ns
		7	RA (RR 0.82 [0.59 to 1.13]) ns

CCT, controlled clinical trial; RCT, randomised controlled trial; AP, acupuncture; Aps, acupressure; ES, non-invasive electrostimulation; EA, electroacupuncture; P, placebo; S, sham; N, nausea; V, vomiting; early, 0–6 h postop; late, 0–48 h postop; acute, 0–24 h postchemotherapy; RA, rescue antiemetics; ns, not significant; pos., positive results; sig, significant; na, not applicable; RR, relative risk; CI, confidence interval; SMD, standardised mean differences.

## Systematic reviews

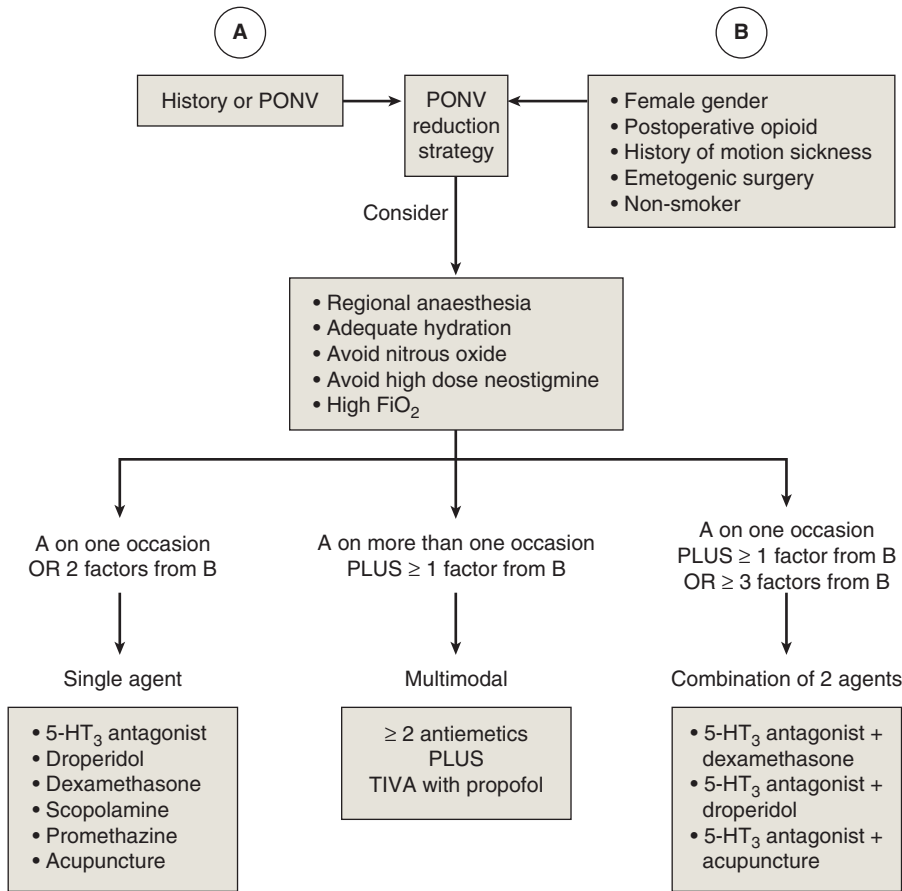
The first review on an antiemetic effect of acupuncture and other stimulation techniques of PC6 was published in 1996 (Vickers, 1996) and included 21 trials for PONV of which 16 showed positive results. However, the methodological limitations and heterogeneity in

TABLE 22.3 ■ Recent RCTs of acupuncture for nausea and vomiting (not reported in previous reviews)

Indication	Reference	n	Intervention	Control	Results
PONV Hysterectomy	Frey et al. (2009b)	200	ES at PC6	S-ES	PONV (sig)* Rescue (sig)*
PONV Cholecystectomy	Frey et al. (2009a)	200	ES at PC6	S-ES	PONV (ns) Early N (sig)*
PONV Breast surgery	Majholm and Møller (2011)	134	Aps at PC6	S-Aps	N (ns) V (ns)
PONV Plastic surgery	Larson et al. (2010)	122	ES at PC6	S-ES (off)	N (sig)*
PONV Supratentorial craniotomy	Wang et al. (2010)	80	ES at PC6	S-ES	N (sig)* V (sig)*
CRNV Breast cancer	Dibble et al. (2007)	160	Self-Aps at PC6	Self-Aps at ST13 Usual care	Acute N (ns) V (ns) Delayed emesis (sig)* Same result
CRNV Breast cancer	Molassiotis et al. (2007)	36	Aps	Usual care	V (sig)*
CRNV Breast cancer	Roscoe et al. (2005)	96	ES at PC6 +SA	S-ES + SA No ES + SA	N (ns), V (ns) N (ns), V (ns)

AP, acupuncture; Aps, acupressure; ES, electrostimulation; EA, electroacupuncture; P, placebo; S, sham; SA, serotonin-antagonist; N, nausea; V, vomiting; sig, significant; ns, not significant.

\* $p < 0.05$  or better.



**Figure 22.4** PONV reduction strategy (Habib and Gan, 2004). TIVA, total intravenous anaesthesia.

the included studies did not allow clear conclusions to be drawn on the efficacy of acupuncture on PONV.

Later a meta-analysis of 19 RCTs seemed to confirm that PC6-stimulation is effective to prevent PONV (Lee and Done, 1999). However, due to the heterogeneity only five studies evaluating early nausea within 6 h postoperatively and eight studies evaluating early vomiting could be included into the meta-analyses which showed effectiveness of acupuncture (see Table 22.2). Those studies only included adults, whereas the four RCTs including children showed no effect. In the other meta-analyses evaluating late nausea and late vomiting, no significant differences could be detected. It is noteworthy that the quality of the study affected the overall result, with poorer studies showing a significant effect. Again, methodological shortcomings and heterogeneity made it difficult to draw clear conclusions.

The same authors subsequently updated their review including 26 trials (Lee and Done, 2004) and later 40 trials involving 4858 participants (Lee and Fan, 2009). In those reviews they did not differentiate between early and late NV but instead used the longest cumulative follow-up data from the end of surgery of NV respectively. In their latest review they found that compared with sham treatment PC6 stimulation significantly reduced nausea, vomiting and the need for rescue antiemetics (see Table 22.2). The effect was similar between children and adults,

and between invasive (acupuncture) and non-invasive (acupressure and ES) modalities. Further they found no evidence of difference between PC6 acupuncture point stimulation and antiemetic drugs in the risk of nausea, vomiting or the need for rescue antiemetics (see [Table 22.2](#)). However, these results should be interpreted with caution because the pooled antiemetics included a variety of drugs including metoclopramide, which is not universally accepted as effective for PONV prophylaxis.

Patient populations at higher risk for PONV had more benefit. For example, if in the control group the PONV rate was 70%, five patients need to be treated in order that one does not suffer from PONV. Thus the number needed to treat (NNT) is 5. If the PONV rate was 30% then the NNT was calculated as 11. In comparing the first and the later reviews of Lee, it might be disappointing to see that the relative risk of nausea or vomiting reduction was nearly halved (see [Table 22.2](#)). This could be explained firstly by combining early and late NV in the later analysis, and secondly by the increasing methodological quality of the later studies, which usually showed smaller differences between the treatment groups.

## Recent RCTs

Of the recent RCTs which were not included in the previously described reviews, the following are noteworthy to summarise briefly (see [Table 22.3](#)).

Electrical stimulation at PC6 reduces early nausea (up to 2h) but not vomiting after laparoscopic cholecystectomy ([Frey et al., 2009a](#)). A significantly lower incidence of PONV and need of rescue therapy in electrical stimulation (current at 31 Hz up to 35 mA) compared to sham stimulation was shown in 200 patients undergoing vaginal hysterectomy ([Frey et al., 2009b](#)). Non-invasive electrical stimulation at PC6 reduced NV significantly compared to sham-point stimulation in patients undergoing supratentorial craniotomy ([Wang et al., 2010](#)) and reduced nausea in outpatients having plastic surgery ([Larson et al., 2010](#)). Tetanic stimulation at PC6 with a neuromuscular monitoring device ([Kim et al., 2011](#)) significantly reduced PONV compared to stimulation at the ulnar nerve.

In contrast to those studies which included ES, a large randomised controlled trial including 134 women undergoing breast surgery found that wristband acupressure at PC6 was not effective ([Majholm and Møller, 2011](#)).

A pragmatic randomised controlled trial showed that acupuncture during anaesthesia combined with postoperative acupressure in children was superior to standard treatment ([Liodden et al., 2011](#)).

Despite the overview of the complete body of studies, which does support antiemetic effects for acupuncture point stimulation, the debate on the evidence for the efficacy of acupressure for preventing PONV is still ongoing ([Streitberger and Kranke, 2011](#)). Although the evidence overall supports the effectiveness of PC6 stimulation in reducing PONV, few current guidelines for the prevention of PONV include acupuncture.

## CHEMOTHERAPY-RELATED NAUSEA AND VOMITING

Chemotherapy regimens often induce NV to a greater or lesser extent. The symptoms can occur within 24 h of chemotherapy (acute) or later than 24 h but less than seven days postchemotherapy (delayed). Despite routinely applied antiemetic drugs before chemotherapy with high risk of emesis (e.g. 5-HT<sub>3</sub> receptor antagonists plus corticosteroids) many patients still suffer from CRNV. Therefore, the need for evaluation of additional ways to reduce these symptoms ([Gralla et al., 1999](#); [Hesketh et al., 1998](#)) has led to interest in non-pharmacological adjuncts to drugs like acupuncture or acupressure. Meanwhile also the body of evidence acupuncture on CRNV has increased notably.

## Systematic reviews

In a review including studies published up to 2005, the pooled results of 11 RCTs evaluating acupuncture point stimulation plus antiemetic drugs for CRNV showed a significant reduction in the proportion of patients experiencing acute vomiting ( $p=0.04$ ), and a trend towards significance for reducing acute nausea severity ( $p=0.1$ ) (Ezzo et al., 2005) (see Table 22.2). This review indicated some differences as a function of modality of stimulation. Acupressure showed a protective effect for both mean acute nausea severity ( $p=0.04$ ) and most severe acute nausea score ( $p=0.03$ ), but not for acute vomiting. None of the pooled studies involved a placebo control. EA showed a benefit of reduced acute vomiting ( $p=0.02$ ), but manual acupuncture did not. For acute nausea, manual acupuncture was equivocal, and no data were reported for EA. Only a few trials had data on delayed NV. They all used non-invasive ES and outcomes were not significantly improved compared to placebo.

One of the main problems in the interpretation of the meta-analyses is the differences in the concomitant antiemetic therapy. For example the negative manual acupuncture trial compared it with modern antiemetic drugs, and the EA trials used older antiemetics which would not be regarded as effective by today's standards.

Within another review on the efficacy of acupuncture point stimulation for the management of therapy related adverse events in patients with breast cancer, 11 trials with mainly positive results were included (Chao et al., 2009). Of those only four were of high quality (Shen et al., 2000; Roscoe et al., 2005; Dibble et al., 2007; Molassiotis et al., 2007). Three of them were not reported in the review by Ezzo, but showed similar results. One study found no difference in the antiemetic effects of non-invasive ES wristbands versus sham for CRNV (Roscoe et al., 2005), one showed a significant difference with acupressure compared to sham only in delayed emesis (Dibble et al., 2007), and one was positive for acupressure on vomiting compared with usual care (Molassiotis et al., 2007) (see Table 22.3).

## PREGNANCY-RELATED NAUSEA AND VOMITING

NV in early pregnancy, which is also described as morning sickness, affects more than 50% of pregnant women in Western societies. Drugs are usually avoided during the critical embryogenic period, because of concerns about their potential teratogenic effects. Therefore, many women seek alternatives such as acupuncture or acupressure.

The first systematic review on acupuncture and NV (Vickers, 1996) suggested that PC6 stimulation also reduces PRNV (see Table 22.3).

Within a further review on alternative therapies for PRNV, six trials with acupressure and one trial with ES were described (Aikins, 1998). Six of them showed at least partially positive results. However, the most methodologically rigorous trial involving 161 patients revealed no differences in PRNV between acupressure and placebo (O'Brien et al., 1996).

The most recent Cochrane review on interventions for NV in early pregnancy (Matthews et al., 2010) included four randomised controlled studies with PC6 acupressure versus placebo, one study with PC6 acupressure versus vitamin B6, one study with auricular acupressure versus placebo, one study with non-invasive ES versus placebo and two studies with acupuncture versus placebo. In none of the studies was a significant difference between groups shown. Only subgroup analyses of some trials showed that the duration, though not the severity, of nausea was significantly reduced with acupressure compared to a placebo band (Norheim et al., 2001), and that acustimulation was more effective than placebo bands in reducing moderate but not severe PRNV (Miller et al., 2001). This Cochrane review also revealed that the effectiveness of all other interventions (ginger, vitamin B6, antiemetic drugs) is limited and not consistent. According to the authors' conclusions there is a lack of high-quality evidence to support any advice on which intervention to use for NV in early pregnancy.

On the subject of the incidence of NV during labour and delivery, in a recent study including 340 women, acupressure wristbands were applied bilaterally at PC6 but showed no greater effect than sham acupressure bands (Sinha et al., 2011).

The swing from positive to negative results in early to later reviews is remarkable, especially regarding the effects of acupuncture point stimulation on PRNV. The effect seemed to depend on the inclusion criteria, as well as the quality and interpretation of the included studies.

Nevertheless, for practical reasons and because of a lack of side effects, PC6 acupressure might be a beneficial, low-cost option for PRNV, even if it is not much more than placebo.

## MOTION-RELATED NAUSEA AND VOMITING

Sea-Bands were originally designed to prevent and treat MRNV at sea. Despite the widespread use of Sea-Bands all over the world, no reviews exist on acupuncture point stimulation for MRNV. Therefore only single trials can be described.

Of five studies of acupressure at PC6, two showed significantly less nausea and also showed less abnormal gastric myoelectric activity compared to sham acupressure and no treatment (Hu et al., 1995; Stern et al., 2001). In the third study, acupressure reduced significantly the time to moderate nausea during eccentric rotation compared to no treatment, but there was no significant difference compared to sham acupressure (Alkaissi et al., 2005). The remaining two studies, with 36 and 18 subjects, respectively, showed no effect of acupressure (Bruce et al., 1990; Warwick-Evans et al., 1991).

One trial of non-invasive ES of PC6 with the ReliefBand® showed a positive effect compared to sham stimulation in a small crossover study of nine healthy volunteers on the open sea (Bertolucci and DiDario, 1995), whereas another study of 77 volunteers showed that PC6 stimulation either by ES or acupressure could not prevent motion sickness induced by optokinetic drum exposure (Miller and Muth, 2004).

Another study which compared Korean hand acupressure at K-K9 with sham acupressure in 100 geriatric patients during ambulance transport (Bertalanffy et al., 2004) showed significant differences in nausea scores and in the overall patient satisfaction.

Due to the heterogeneity of those studies with conflicting results no conclusion on the efficacy of acupuncture point stimulation on motion MRNV is possible. However, as was suggested for PRNV it might be reasonable to propose the use of acupuncture point stimulation on MRNV for practical reasons.

## Concluding comments

Of the four NV-related conditions described in this article, the evidence is most robust with respect to PONV. Data show that PC6 reduces the risk of both NV, with an effect similar to medication; that benefits are consistent for both children and adults, and that invasive and non-invasive modalities are equally effective. Given this, the least invasive modality such as acupressure bands or ES wristwatch-like devices could be selected. For an experienced acupuncturist, application of manual acupuncture at PC6 just before induction of anaesthesia might be the best way to achieve PONV prophylaxis. The effect might be enhanced by electrical stimulation or use of additional acupuncture points like ST36. Because they are time consuming, these methods might not be applicable routinely in the perioperative setting. The recently described positive results of electrical stimulation with neuromonitoring devices (Arnberger et al., 2007; Kim et al., 2011) might encourage anaesthetists to include this easily applicable method into the routine for patients with high risk for PONV. Most PONV trials to date have focused on PC6 without additional antiemetic medication. Future PONV trials should ascertain whether acupuncture point stimulation *plus* medication is superior to either alone, especially for those patients at highest risk.

For CRNV, acupressure appears to reduce chemotherapy-induced acute nausea but not vomiting and, therefore, might offer a low-cost, convenient, self-administered intervention for chemotherapy patients to reduce nausea on the first day. However, as these trials lacked a sham control, placebo effects cannot be ruled out. For CRNV acute vomiting, only EA was effective. However, while the effectiveness of EA provides proof of principle, studies that combine EA with state-of-the-art antiemetics are needed to determine whether EA can confer additional benefit to modern antiemetics and in refractory patients. The most conflicting results emerge in reviews of PRNV where only a few subgroup analyses showed a protective effect of PC6 stimulation.

Additional questions remain (Streitberger and Kranke, 2011). What is the optimal site of stimulation? PC6 is the most highly documented point, but auricular acupuncture or Korean hand acupuncture may be promising alternatives or adjuncts. Other acupuncture points such as ST36 might be helpful adjuncts to PC6 but need more investigation.

What is the optimal time of stimulation? For the prevention of PONV, stimulation should ideally be performed before induction of anaesthesia to enhance psychological effects. However, it is possible that treatment afterwards might sometimes be a better option, especially for children or patients with needle phobia. For CRNV, stimulation is mostly performed before the application of chemotherapy and is repeated in between the treatments. For motion- and pregnancy-related NV, treatment with stimulation bands can be used prophylactically or after onset of first NV.

Further large, high-quality clinical trials are important to identify the clinical value of the method, the most practical and effective techniques, and identification of the kinds of patients who will benefit most.

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## Acupuncture in cardiovascular medicine

J.C. Longhurst

### CHAPTER OUTLINE

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### Introduction

Although acupuncture is an ancient discipline in traditional Chinese Medicine (TCM) only in the last few decades has modern science begun to provide mechanistic insights into its clinical actions. From the early 1970s till the late 1990s there were over 500 randomised controlled clinical trials investigating the clinical influence of acupuncture (Klein and Trachtenberg, 1997; Vickers, 1998), yet a beneficial action has been proven rigorously for very few diseases. Since then, the number of articles published on acupuncture research (451 articles worldwide in 2009) has been increasing almost exponentially, with the US and China both taking lead roles in advancing our understanding of this ancient therapy (Han and Ho, 2011). Cardiovascular disease and its attendant symptoms, most notably hypertension and angina pectoris, represent new areas for which there is mounting evidence that acupuncture can be used successfully in treatment (World Health Organization, 2003). However, there is a strong rationale for achieving a better understanding of the clinical actions of acupuncture in translational studies as well as at the organ system, cellular

and subcellular levels. Such information has the potential to influence attitudes and potential acceptance of this therapeutic strategy by the Western medical and scientific communities who in the past have been reluctant to incorporate acupuncture into their curricula, clinical practice or research investigation. This chapter reviews our current understanding of the cardiovascular actions of acupuncture from both experimental and clinical perspectives.

## **Mechanisms of action of acupuncture in cardiovascular regulation**

Early investigations of acupuncture's action on blood pressure, for example experimental hypertension, described the importance of the central nervous system (CNS) in mediating its physiological and clinical responses (Li and Yao, 1992). Over the last two decades, animal studies in both China and the United States have identified many of acupuncture's mechanisms of action on cardiovascular function (Li and Longhurst, 2010; Lin et al., 2001; Longhurst, 1998, 2002, 2011; Longhurst and Costello, 2011).

### **MERIDIANS ARE NEURAL PATHWAYS**

Meridians and acupuncture points represent a road map that traditionally guided acupuncturists where to stimulate along the body surface to evoke clinically meaningful responses (Li P. et al 2012; Longhurst, 2010a). Substantial evidence shows that neural pathways are responsible for the action of acupuncture. In this regard, the only constant anatomical structures located in the vicinity of acupuncture points are nerves and nerve endings (Yu et al., 1996). Local anaesthetic infusion into the region of the acupuncture point – but not inflation of a blood pressure cuff to supra-systolic pressures to stop blood flow – interrupts acupuncture analgesia (Chiang et al., 1973; Han, 1987). There is some disagreement in the literature with regard to the role of afferent versus efferent fibre stimulation in acupuncture's clinical responses (Kline et al., 1978). However, specific interruption of sensory rather than motor nerve fibres by transection abolishes acupuncture modulation of excitatory cardiovascular responses, since motor paralysis does not influence acupuncture's action (Tjen-A-Looi et al., 2012). Furthermore, the important role of somatic sensory nerve fibre stimulation in acupuncture-cardiovascular modulation is underscored by the clinical observation of acupuncturists that the neural sensation or paraesthesia representing *de qi*, described as a burning sensation, a fullness or heaviness in the region of acupuncture application, is often associated with optimal clinical responses.

### **MANUAL VERSUS ELECTROACUPUNCTURE**

Most acupuncturists employ manual acupuncture during which needles are inserted, then left in place or intermittently rotated and frequently moved up and down to strengthen the acupuncture response. Electroacupuncture (EA) is commonly used experimentally since this form of acupuncture is easily standardised, for example continuous stimulation at 2 Hz for 30 min. The cardiovascular depressor responses to manual and EA are virtually identical because both forms of stimulation, when matched for frequency of stimulation (2 Hz), cause very similar activation of somatic sensory nerves (Zhou et al., 2005).

#### **High versus low frequency EA**

Both low and high frequency EA (2 and 100 Hz) have been reported to be efficacious in studies of acupuncture analgesia (Han, 2011; Wang et al., 1992). However, low frequency (2 Hz) EA at PC5 and PC6 acupuncture points over the median nerves reduces sympatho-excitatory blood pressure responses much more than high frequency (100 Hz) EA since there is much greater activation

of afferent fibres during low compared to higher frequencies of stimulation (Zhou et al., 2005). Most studies employing EA to modulate cardiovascular function therefore have employed low frequency stimulation, frequently stimulating acupuncture points bilaterally.

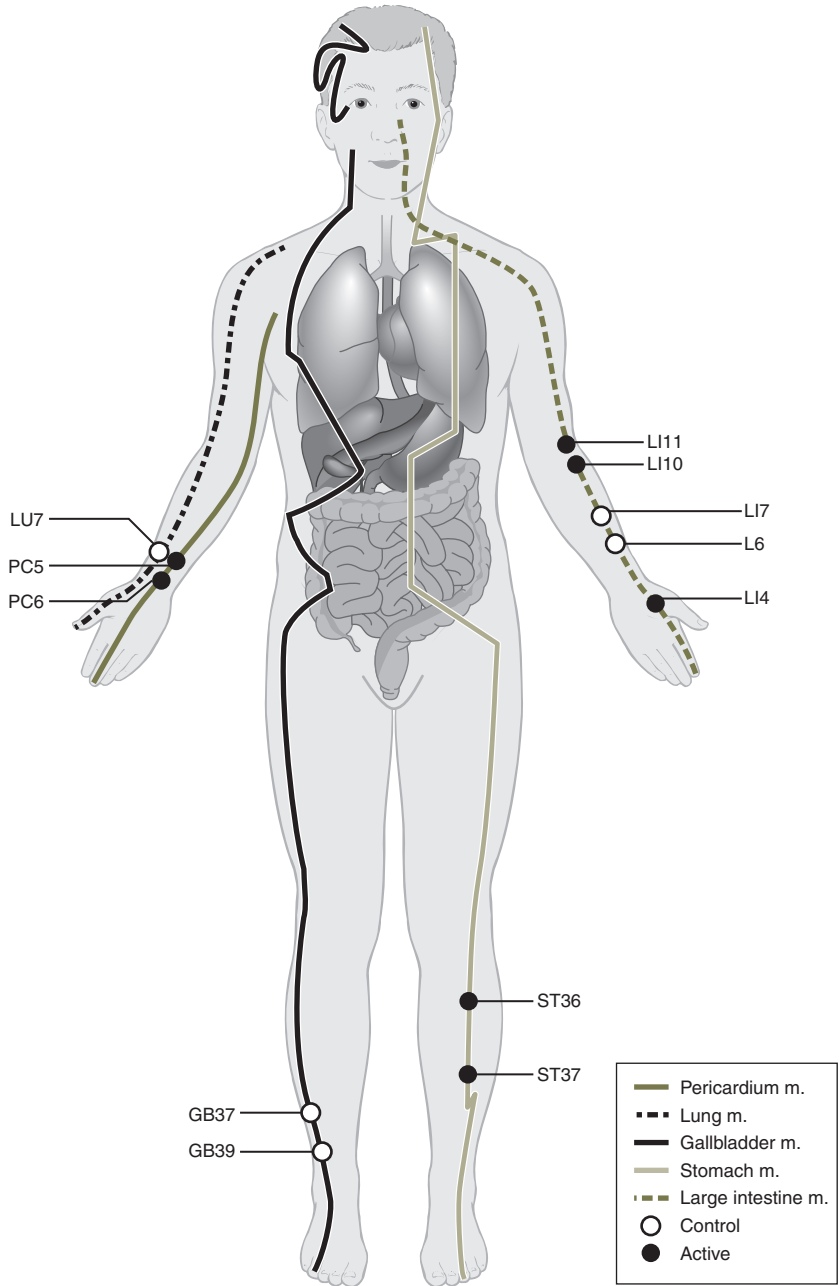
## POINT SPECIFICITY

The concept of point specificity is controversial. It implies that stimulation of some acupuncture points is more effective, at least in certain clinical conditions such as hypertension, whereas other points are less effective or are ineffective (Choi et al., 2012). The term implies that the needle must stimulate a particular tissue to elicit a particular physiological effect, rather than that the needle has to be inserted precisely at a tiny location shown on a chart. A systematic review of 12 studies asking the question ‘are acupuncture points specific for diseases?’ concluded that approximately half of the trials found evidence for point specificity and half did not (Zhang et al., 2010). However, a number of trials included in this review were at risk of bias. Six with a low risk of bias (as assessed by the Cochrane Collaboration tool for assessing bias risk) showed no difference between non-point and true acupuncture stimulation, thus suggesting that point specificity is not real.

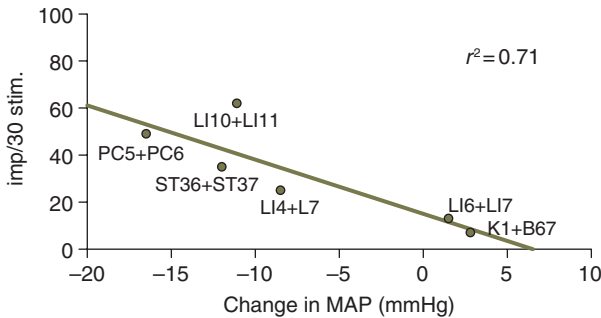
An argument for the existence of point specificity has been made by Han, who argues that the uneven distribution of nerves in the body should yield point specific responses to needling different acupuncture points (Han, 2011). Studies in humans confirm such specific responses to exercise-induced elevations in blood pressure (Li et al., 2004). Point specific cardiovascular hypotensive responses in reflex-induced hypertension are observed experimentally when EA is applied at different acupuncture points, with some points resulting in significant reductions in elevated blood pressure and others causing more modest responses or no change at all (Tjen-A-Looi et al., 2004). Thus, stimulation of acupuncture points (PC5, PC6, ST36, ST37, LI4, LI10 and LI11, Fig. 23.1) located over deep somatic nerves such as the median and deep peroneal nerves reduces reflex elevations in blood pressure much more than EA at other acupuncture points (LI6, LI7, KI1 and BL67, see Fig. 23.1) located over superficial (cutaneous) pathways like the superficial radial and tibial nerves. Studies to evaluate the mechanism of point specific cardiovascular depressor responses show that stimulation of nerves underlying acupuncture points, capable of reducing elevated blood pressure the most, evokes the highest discharge in the rostral ventrolateral medulla (rVLM), a brain stem region that significantly regulates premotor sympathetic outflow (Fig. 23.2). Thus, ‘hard wiring’ of somatic nerves that indirectly project to cardiovascular regions of the brain capable of lowering elevated blood pressure during stimulation of certain ‘cardiovascular’ acupuncture points provides an anatomical explanation for point specificity.

## OPTIMAL SELECTION OF ACUPUNCTURE CONTROL POINTS

Observations from studies of point specificity have implications for selection of effective controls for past and future experimental and clinical studies of acupuncture and its actions on the cardiovascular system. In this regard, either (a) inactive acupuncture points or (b) active acupuncture points in which a needle is placed but not stimulated can serve as two strong controls to be compared with responses to stimulation of active cardiovascular acupuncture points (Zhou et al., 2005). Inactive points provide little input to cardiovascular centres of the brain while (b), the second option, fails to evoke sufficient sensory input during acupuncture to modulate cardiovascular function (Li M. et al., 2010; Li et al., 2004, 2006; Zhou et al., 2005). However, with both types of control, meridians and acupuncture points are targeted, and during stimulation of inactive acupuncture points there is the potential for *de qi* to develop. If the acupuncturist is not informed which set of acupuncture points have the potential to exert strong cardiovascular



**Figure 23.1** Acupuncture points grouped by those demonstrated to exert strong cardiovascular action when stimulated (active points) and those that cause no cardiovascular response and which can be used as control points in studies of acupuncture regulation of the cardiovascular system. See text for additional discussion. (Reproduced from Li, P., Longhurst, J.C., 2010. Neural mechanism of electroacupuncture's hypotensive effects. *Auton. Neurosci.* 157, 24–30, with permission of Elsevier.)



**Figure 23.2** Relationship between changes in mean arterial blood pressure (MAP) and evoked activity in the rostral ventrolateral medulla (rVLM) during electroacupuncture modulation of visceral sympathoexcitation. Electroacupuncture at each set of acupuncture points was maintained at low frequency (2 Hz) for 30 min, while evoked activity in the rVLM was measured, during needle stimulation at the same acupuncture points and frequency for 15 s. A strong correlation was observed between acupuncture points that evoked large increases in rVLM activity (measured as the number of evoked responses or impulses for 30 acupuncture point stimulations) and decreases in the reflex increases in MAP (e.g. PC5 and PC6) as well as those that evoked little activity in this medullary region and did not influence the reflex sympathoexcitation, indicating that acupuncture points overlying nerves that project to a region of the brain that is known to regulate sympathetic activity are most capable of influencing cardiovascular function through their actions on autonomic outflow. See Figure 23.1 and text for explanation of acupuncture point nomenclature. (Reproduced from Tjen-A-Looi, S.C., Li, P., Longhurst, J.C., 2004. Medullary substrate and differential cardiovascular response during stimulation of specific acupuncture points. *Am. J. Physiol.* 287, R852–R862, with permission of the American Physiological Society.)

autonomic modulation, it is possible to conduct a double blind study, a difficult proposition in many acupuncture trials, since therapists typically are not blinded.

## CARDIOVASCULAR RESPONSES TO STIMULATION OF ACUPUNCTURE POINT COMBINATIONS

Clinical acupuncture typically involves stimulation of a number of acupuncture points in combination to reinforce and increase acupuncture's action (Ulett et al., 1998; Zhou et al., 2005). Older studies suggest that manual stimulation of two points, e.g. LI4 and ST36, leads to greater analgesia than needling one point (Research Group AABMC, 1973). For safety, EA typically involves stimulating at least two closely associated acupuncture points, such as PC5 and PC6, since the negative and positive leads of the stimulator are connected separately to each of the two needles. This configuration allows current to flow locally between the two electrodes, frequently through the underlying low resistance nerve bundle. It is preferable to avoid current flow across the body and potentially through the heart (where electrical activity could be altered), which occurs when the same acupuncture point is stimulated bilaterally, one needle connected to the positive lead and the needle in the contralateral acupuncture point connected to the negative lead.

The additive influence resulting from stimulation of different combinations of acupuncture points during EA has been brought into question when the magnitude and frequency of stimulation and hence summated input into the CNS are precisely controlled. In this regard, bilateral stimulation of two combinations of acupuncture points (PC5 + PC6 and ST36 + ST37, using eight needles) that independently exert strong cardiovascular responses (Tjen-A-Looi et al., 2004) does not evoke larger decreases in elevated blood pressure than stimulation of individual sets of acupuncture points (Zhou et al., 2005). As such, available data on the cardiovascular influence of EA does not support using more than one set of acupuncture points stimulated bilaterally. On the other hand, because there is a potential for

local, regional and systemic actions of acupuncture, more studies on the potential additive or synergistic effects of stimulating combinations of acupuncture points to maximise clinical responses are needed.

## BRAIN STEM NEUROTRANSMITTER MECHANISMS IN ACUPUNCTURE'S CARDIOVASCULAR ACTION

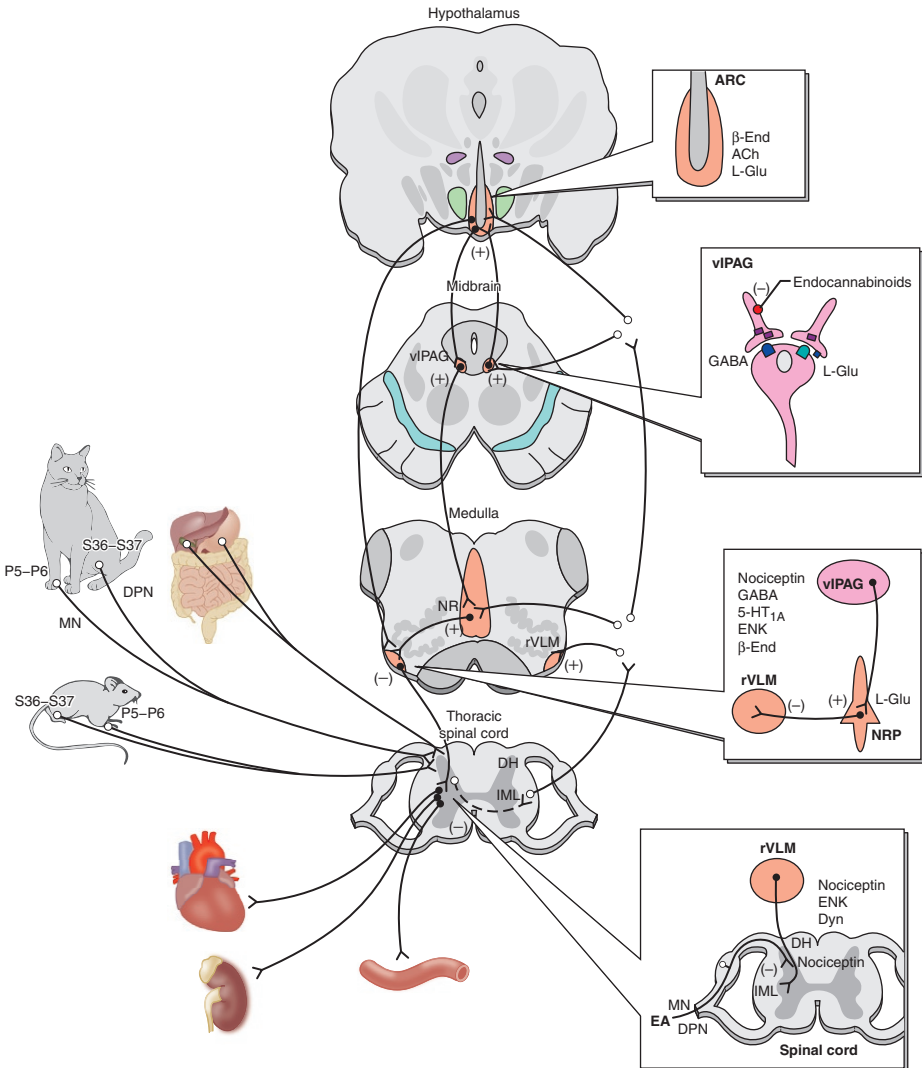
Acupuncture regulates cardiovascular function, at least in part, through its actions on sympathetic and parasympathetic outflow. Several neurotransmitter systems, including opioids,  $\gamma$ -aminobutyric acid (GABA) and serotonin (5-hydroxytryptamine, 5-HT) in the rVLM (Li et al., 2001; Moazzami et al., 2010; Tjen-A-Looi et al., 2003, 2006, 2007), participate in regulation by acupuncture of experimental reflex-induced and central neurogenic hypertension (Huangfu and Li, 1988; Li and Yao, 1992; Zhang et al., 1992). Anatomical studies employing c-Fos, a marker of CNS neuronal activation during EA, demonstrate enkephalins in cell bodies of rVLM neurons that process somatic afferent signals during EA, and show that  $\beta$ -endorphin is present in closely located axons (Guo et al., 2004; Li et al., 2009). Opioid  $\mu$ - and  $\delta$ - and, to a significantly lesser extent,  $\kappa$ - receptors mediate EA modulation of sympatho-excitatory reflex responses (Li et al., 2001), indicating that  $\beta$ -endorphin (and possibly endomorphin) and enkephalins, but less likely dynorphin, are involved in rVLM processing of somatic afferent input during EA. The rVLM and possibly the nucleus raphé pallidus (NRP) appear to be the sources of enkephalins that act in the rVLM during EA (Guo and Longhurst, 2007; Guo et al., 2004), while  $\beta$ -endorphin is produced in the arcuate nucleus of the hypothalamus and is transported through long projections to the rVLM where it acts (Guo and Longhurst, 2007; Guo et al., 2004; Li et al., 2009). Thus EA, through opioid and non-opioid mechanisms, inhibits the release of the excitatory neurotransmitter glutamate in the rVLM, which is responsible for visceral reflex-related increases in sympathetic outflow and blood pressure (Zhou et al., 2007).

## LONG-LOOP PATHWAY IN ACUPUNCTURE'S CARDIOVASCULAR ACTIONS

Although brief somatic nerve stimulation, which occurs early during EA, can activate neurons in the rVLM (Sato and Schimdt, 1987; Tjen-A-Looi et al., 2003), it is the more prolonged stimulation of somatic nerves lasting for at least 10–15 min during acupuncture that activates a 'long-loop' pathway and leads to opioid-mediated regulation of premotor sympathetic neurons in this cardiovascular brain stem region (Li et al., 2009).

The long-loop pathway involved in the acupuncture-cardiovascular response consists of the arcuate nucleus in the ventral hypothalamus (Cheung et al., 2001; Guo and Longhurst, 2007; Li P. et al., 2012; Li and Yao, 1992), the ventrolateral periaqueductal grey (vlPAG) in the midbrain (Guo and Longhurst, 2010; Guo et al., 2004; Li P. et al., 2010a), the NRP (Guo et al., 2008; Li et al., 2006, 2009, Li P. et al., 2010b) in the midline medulla and the rVLM that collectively are responsible for prolonged EA modification of sympatho-excitatory reflex cardiovascular responses (Fig. 23.3).

Acupuncture's cardiovascular actions in the long-loop pathway are mediated by a number of excitatory and inhibitory neurotransmitter systems including *glutamate* acting through both N-methyl-D-aspartate (NMDA) and non-NMDA or  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid ionotropic receptors in the arcuate and vlPAG (Li P. et al., 2010a,b); acetylcholine through a *muscarinic cholinergic* mechanism in the arcuate (Li P. et al., 2010a); *endocannabinoids* that, through a presynaptic CB1 mechanism, reduce the release of *GABA* to disinhibit vlPAG neurons (Fu and Longhurst, 2009; Tjen-A-Looi et al., 2009); *serotonin* through a 5-HT<sub>1A</sub> mechanism in NRP neurons that project to the rVLM (Moazzami et al., 2010); as well as *opioids* (see the preceding text), *GABA* and *nociceptin* in the rVLM (Crisostomo et al., 2005; Tjen-A-Looi et al., 2007).



**Figure 23.3** Neural circuitry of acupuncture's action on visceral reflex-induced changes in cardiovascular sympathetic outflow following application of bradykinin (BK) to the gallbladder of cats or distension of the stomach in rats. Electroacupuncture at PC5 + PC6 and ST36 + ST37 somatic acupuncture points stimulates the median (MN) and deep peroneal nerves (DPN) evoking activity in the arcuate nucleus (ARC) in the ventral hypothalamus, ventrolateral periaqueductal grey (viPAG) in the midbrain, nucleus raphé (NR) especially the NR pallidus (NRP) and rostral ventrolateral regions of the medulla (rVLM) as well as the dorsal horn (DH) and intermediolateral column (IML) of the spinal cord. A number of neurotransmitters, including acetylcholine (ACh), L-glutamate (L-Glu),  $\beta$ -endorphin ( $\beta$ -End), endocannabinoids,  $\lambda$ -aminobutyric acid (GABA), met- and leu-enkephalin (Enk), serotonin or 5-hydroxytryptamine (5-HT), nociceptin and dynorphin (Dyn) in the brain and spinal cord have been shown to participate in these brain nuclei by either activating (+) or inhibiting (–) neural activity evoked by the primary visceral reflex during EA modulation. The long pathway between the ARC and the rVLM illustrates the primary source of  $\beta$ -End. See text for details. (Reproduced from Li, P., Longhurst, J.C., 2010. Neural mechanism of electroacupuncture's hypotensive effects. *Auton. Neurosci.* 157, 24–30, with permission of Elsevier.)

## SPINAL MECHANISMS OF TRANSCUTANEOUS ELECTRICAL AND MAGNETIC STIMULATION AND ACUPUNCTURE

There are similarities between transcutaneous electrical nerve stimulation (TENS) and EA ([Melzack and Wall, 1982](#)). TENS is not exactly equivalent to acupuncture since much stronger intensities of stimulation and higher frequencies are commonly used during transcutaneous stimulation that are not directed at specific locations (acupuncture points). However, like TENS ([Melzack and Wall, 1984](#)), other acupuncture surrogates such as transcutaneous magnetic stimulation as well as EA appear to ‘close the gate’ at spinal and supraspinal levels by preventing the central transmission of impulses to the CNS, since sensory activation during both TENS and EA provides convergent input to common interneurons responsible for central neurotransmission of cardiovascular excitatory reflexes. For example, transcutaneous low frequency pulsed electromagnetic stimulation in rats leads to acupuncture-like inhibition of visceral sympatho-excitatory blood pressure responses through a naloxone-sensitive mechanism at the spinal level ([Zhou et al., 2006](#)). Enkephalins and dynorphin predominate in spinal processing of cardiovascular responses since the modulatory influence of magnetic stimulation is blocked by  $\delta$ - and  $\kappa$ -, but not  $\mu$ -opioid antagonists administered intrathecally ([Zhou et al., 2006](#)). Conventional EA likewise reduces visceral sympatho-excitation through both naloxone-sensitive opioid and non-opioid (nociceptin) mechanisms in the spinal cord dorsal horn and intermediolateral column (IML) ([Zhou et al., 2009](#)). Actions by enkephalins, dynorphin and nociceptin in the dorsal horn imply that EA inhibits sensory inflow, while EA’s action in the IML indicates that it modulates sympathetic outflow. These data demonstrate that, in addition to acupuncture’s well-known CNS actions, EA has a well defined regional or segmental action.

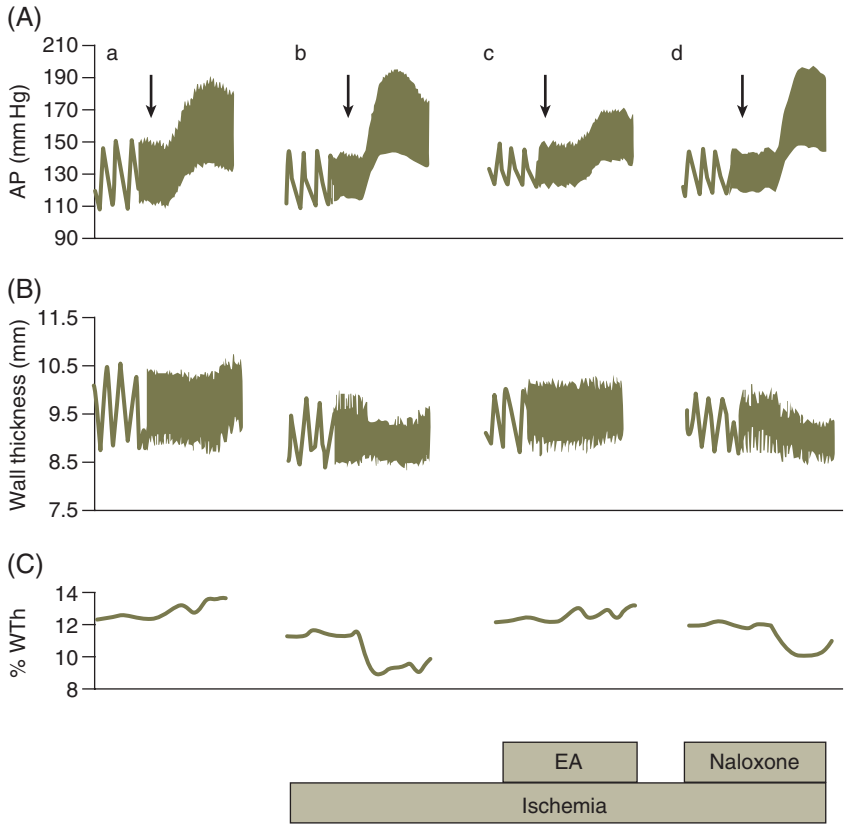
## Clinical effects on cardiac blood supply

### MYOCARDIAL ISCHAEMIA

Experimental and clinical studies suggest that acupuncture can reduce myocardial ischaemia. Through an opioid mechanism, low frequency EA at PC5 and PC6 or direct median nerve stimulation lowers myocardial oxygen demand and hence reduces demand–supply imbalance and regional ventricular dysfunction in experimental myocardial ischaemia ([Chao et al., 1999](#); [Li et al., 1998](#); [Fig. 23.4](#)).

Patients with coronary artery disease frequently experience myocardial ischaemia and angina pectoris during stress. High frequency TENS at 150 Hz with electrodes placed in the same dermatome on the centre of the chest and back of subjects without disease reduces the increase in diastolic blood pressure during isometric exercise, but not during the Valsalva manoeuvre, cold face stimulation or tilt ([Sanderson et al., 1995](#)). Similarly mid frequency TENS (60 Hz) to a level just below motor threshold with electrodes placed over muscle blunts sympathetically mediated reflex pressor responses to handgrip static (isometric) exercise when TENS is applied to the ipsilateral forearm but not when it is applied to the contralateral leg ([Hollman and Morgan, 1997](#)). These data support a segmental (likely spinal) but not a systemic action of TENS on the exercise pressor reflex. The absence of an action of TENS on other sympatho-excitatory reflexes that have the potential to precipitate angina is puzzling. Although preliminary, these data, in aggregate, suggest that TENS might be able to ameliorate heightened sympathetic activity associated with exercise and hence might be a potential therapy for patients with ischemic heart disease.

Several small clinical studies demonstrate that both TENS and acupuncture reduce myocardial ischaemia during pacing and exercise in patients with angina and electrocardiographic (ECG) evidence of ischaemia ([Ballegaard et al., 1990, 1991, 1995, 1996, 1999](#); [Emanuelsson et al., 1987](#); [Mannheimer et al., 1982, 1985, 1989](#); [Richter et al., 1991](#)). A number of other studies published in Chinese on the influence of acupuncture in patients with symptomatic coronary disease are available but were not reviewed for this chapter.

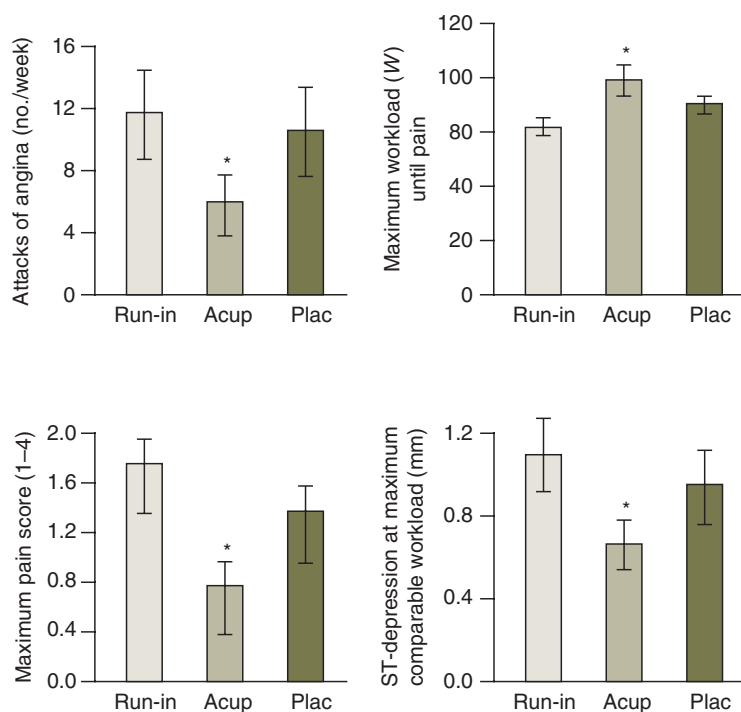


**Figure 23.4** Reflex increases in arterial blood pressure (AP, Panel **A**) and regional myocardial wall thickening measured with a sonomicrometer (Panel **B**). Beat by beat percent wall thickening (% WTh) also was calculated (Panel **C**). Bradykinin (BK) was applied to the gallbladder (arrows) to evoke visceral sympathetic reflex increases in AP and myocardial function (Panel **a**). Following partial occlusion of a small branch of the left anterior descending coronary artery (LAD) (Panel **b**) BK increased AP but reduced WTh, signifying regional ischaemia (Panel **b**). Thirty minutes of electroacupuncture (EA) applied bilaterally at Neiguan and Jianshi acupuncture points (PC5 and PC6, see Fig. 23.1) on the forelegs diminished the reflex increase in AP and reversed the ischemic response (Panel **c**) while intravenous naloxone (Panel **d**) eliminated the action of EA on both AP and regional function. EA therefore is capable of reversing demand-induced myocardial ischaemia through an opioid-sensitive mechanism. (Reproduced from Chao, D.M., Shen, L.L., Tjen-A-Looi, S.C., Pitsillides, K.F., Li, P., Longhurst, J.C., 1999. Naloxone reverses inhibitory effect of electroacupuncture on sympathetic cardiovascular reflex responses. *Am. J. Physiol.* 276, H2127–H2134, with permission of the American Physiological Society.)

Like its action on hemodynamic responses to static exercise, TENS applied to the chest at non-specific points (position of greatest pain) in patients with pacing-induced angina for 20–30 min using 70 Hz cutaneous stimulation at an intensity just below the pain threshold (15–50 mA) at comparable heart rates (HR) reduces systolic blood pressure (SBP), double product (SBP·HR, index of myocardial oxygen demand), angina, ECG ST segment depression and lactate production through a mechanism that is insensitive to a single intravenous (IV) dose of naloxone (Mannheimer et al., 1985, 1989). Additionally, TENS applied repetitively over a 10-week period for 1 h three times daily reduces the frequency of angina and consumption of nitroglycerin (Mannheimer et al., 1985). Maximal exercise capacity is improved with chronic TENS as is ST segment depression. HR and double product, but not SBP at maximal exercise, are reduced by chronic TENS compared to a control group.

An early acupuncture study (Richter et al., 1991) evaluated 21 patients with well-characterised angina who were experiencing chest pain at least five times each week. A cross-over design was used comparing a tablet placebo to manual acupuncture performed three times weekly for 4 weeks using TCM principles (pattern diagnosis) at several main points, including PC6, HT5, BL5, BL20 and ST36. Additional points included HT7, LI4, LI11 and LR3. Needles were manipulated immediately after insertion to achieve *de qi* after which there was no further stimulation. Compared to pretreatment and a tablet placebo, acupuncture increased bicycle exercise workload at the onset of angina (but not the maximal workload) and reduced the number of angina attacks per week, intensity of pain and ECG ST segment depression at maximal workload (Fig. 23.5). Antianginal medication remained constant over the duration of the study. A quality of life questionnaire showed improved feeling of well being. This small study incorporating a suboptimal placebo intervention suggests, through several different measures, that manual acupuncture can decrease myocardial ischaemia and angina. Although there is some debate about whether acupuncture increases coronary blood flow, it clearly can lower the increase in blood pressure and double product (but not the elevated HR) associated with exercise, hence reducing myocardial oxygen demand (Li et al., 2004).

Several other small studies on the influence of manual and EA in normotensive patients with severe stable angina pectoris have been conducted by Ballegaard and co-workers. Exercise responses following 3 weeks of manual acupuncture (seven treatments) without needle



**Figure 23.5** Clinical responses of a small group of patients to manual acupuncture applied using pattern diagnosis over a 4-week period. Compared to control (run-in) and a tablet placebo, acupuncture significantly (\*) reduced the number of attacks of angina, maximum workload achieved and pain score during exercise as well as ECG ST segment depression. Means and standard deviations are shown. (Reproduced from Richter, A., Herlitz, J., Hjalmarson, A., 1991. Effect of acupuncture in patients with angina pectoris. *Eur. Heart J.* 12, 175–178, with permission from Oxford University Press.)

manipulation at PC6, ST36 and BL14, which led to *de qi*, were compared to sham stimulation (outside meridians, same dermatome) in 26 patients with medically refractory angina, a positive stress test and >50% angiographic coronary stenosis (Ballegaard et al., 1986). The investigators found improvement in the change in double product from baseline as well as the maximal double product in the acupuncture but not in the sham group. Conversely, they found no change in anginal attack rate or nitroglycerin consumption. They concluded that improvement was limited possibly by the advanced nature of the disease and the small number of patients studied. The non-aggressive treatment protocol that did not include needle manipulation or EA also may have limited clinical responses in these patients. A second study of 49 patients with moderate stable angina randomised to either acupuncture (using a similar protocol as in the earlier study) or sham stimulation from the same group of investigators demonstrated increased exercise tolerance and delay in onset of pain only in the acupuncture group (Ballegaard et al., 1990). Both sham and acupuncture patients displayed a 50% decrease in angina attacks and nitroglycerin consumption. The greater action of acupuncture in the second study compared to the first may have been due to the less severe nature of the angina (moderate vs. severe). Similar clinical responses in the acupuncture and sham groups argue against point specificity and indicate similar actions of both interventions – both active or both placebo. The small number of patients in each group also limits firm conclusions that can be drawn from this study. A third study from this group involved a course of 50 min of low frequency (2 Hz) EA therapy at LI4 or sham acupuncture (outside meridians, same dermatome) employed three times weekly over a period of 3 weeks in a small group of 33 patients with stable angina and a positive exercise stress test (Ballegaard et al., 1991). They observed decreased nitroglycerin consumption and rate of anginal attacks (Ballegaard et al., 1990, 1991; Liu et al., 1986). Individuals demonstrating an increase in skin temperature of the index finger, which was interpreted to signify vasodilation, appeared to be more responsive to the intervention (Ballegaard et al., 1991). Similar clinical responses to LI4 and sham EA suggests a segmental, non-point specific action of EA.

Ballegaard also has incorporated acupuncture into lifestyle programmes for patients with ischemic heart disease. A 2-year prospective non-randomised study included 69 patients in whom acupuncture followed by acupressure was administered as part of a lifestyle programme incorporating stress reduction, Shiatsu massage and healthy eating. They documented decreases in medication usage, inpatient days and the accumulated mortality rate (Ballegaard et al., 1996). Importantly, postponement of invasive treatment including bypass grafting and transluminal angioplasty in 61% of patients resulted in a 90% decrease in hospital days and a saving of approximately \$12 000 in each patient (Ballegaard et al., 1996). Interestingly, despite more scepticism about acupuncture in men, there were similar clinical responses in both sexes. A follow-up non-randomised comparative 5 year study evaluated 105 patients with severe angina who were treated with acupuncture and self-care education (Ballegaard et al., 1999). The estimated cost saving was \$32 000 per patient over the 5 years of the study, resulting from a 90% reduction in hospitalisation and 70% reduction in surgery, without increased risk for infarction or cardiac death. A third study from this group lasted 3 years and included 168 patients with angina, 103 of which were candidates for invasive treatment, including bypass grafting or angioplasty (Ballegaard et al., 2004). An integrated programme that included acupuncture, self-care acupressure, Chinese health philosophy, stress management and lifestyle modification was calculated over the 3 years to reduce costs by \$36 000 and \$22 000 for surgical and non-surgical patients, principally through reduced invasive treatment and in-hospital days. The specific contribution of acupuncture to these beneficial responses has not been determined.

For angina pectoris, the preponderance of experimental animal and several small clinical studies suggests a beneficial effect of acupuncture and TENS in patients with symptomatic coronary disease who experience demand-induced ischaemia. By reducing myocardial oxygen demand acupuncture lessens supply–demand imbalance and hence angina. Part of acupuncture's antianginal

effect could be simply through its well-known analgesic actions. There is variability between studies, both in application of acupuncture and in the sham controls. Similar responses in sham and control subjects in some studies indicate that placebo actions participate in some of the clinical responses. More research in this area is warranted. Many issues that should be addressed in future studies include, among others, numbers of subjects (since only about 70% of subjects are responsive), blinding of patients (since it is unlikely that practitioners can be blinded), stimulation modality (aggressive manual vs. EA and frequency of stimulation), acupuncture points stimulated, type of sham controls and standardised versus pattern diagnosis approaches to acupuncture point selection.

## MYOCARDIAL INFARCTION

If acupuncture reduces myocardial ischaemia, it is natural to suggest that this intervention also may reduce infarction. Two recent experimental studies examining the potential for EA to reduce infarct size in models of ischaemia-reperfusion injury have arrived at different conclusions. One study of rabbits subjected to 30 min of left anterior descending coronary artery occlusion followed by 90 min of reperfusion reported that 30 min of low frequency (2 Hz) EA (PC5 and PC6), but not sham acupuncture (needle insertion at active points without stimulation), decreased infarct size from 49% to 15% of the area at risk and arrhythmia score in association with a lower HR, double product, ST depression and interstitial norepinephrine concentration during reperfusion (Zhou et al., 2012). Naloxone attenuated the beneficial response to EA. A second trial in rats also employing low frequency (2 Hz) EA (PC5 and PC6) beginning 5 min before occlusion and lasting for 40 min demonstrated no reduction of infarction in the area at risk nor any change in arrhythmias (Kloner et al., 2012). The investigators in the latter study noted no change in hemodynamic responses during ischaemia-reperfusion in response to acupuncture, suggesting that, in the absence of any hemodynamic change, EA is unlikely to alter infarct size. No clinical studies of acupuncture's influence on infarct size have been reported.

## Cardiovascular Risk

A number of cardiovascular risk factors that lead to cardiovascular disease, including hypertension, obesity, hypercholesterolemia and smoking potentially might be influenced by acupuncture. In addition, acupuncture may be efficacious in treating arrhythmias, stroke and peripheral vascular disease (Longhurst, 2007a,b), although clearly more studies are warranted.

## SYMPATHETIC ACTIVITY AND SKIN TEMPERATURE IN HUMANS

As noted earlier, experimental studies have shown that acupuncture regulates acute reflex-induced elevations in blood pressure by modulating sympathetic outflow. However, variable responses of human muscle sympathetic nerve activity (MSNA) and surrogate measures of sympathetic activity to acupuncture (e.g. skin temperature) have been reported (see also Chapter 6). Indirect measures of cutaneous sympathetic activity, such as skin thermography, have demonstrated a consistent generalised warming effect, greatest on the face and least on the feet, during manual or low frequency EA at ST36 or LI11 (Ernst and Lee, 1986). Like the increases in temperature noted in the preceding text by Ballegaard et al. (1991), the warming was interpreted to represent systemic decreases in sympathetic outflow and vasodilation.

In fact, changes in skin temperature have been used to identify individuals who might respond to acupuncture (Ballegaard et al., 1991). It would be useful to identify responsive and non-responsive individuals since, as noted earlier, the influence of acupuncture occurs in

only 70% of individuals (Middlekauff et al., 2001). In this regard, individuals demonstrating changes in pain threshold and skin finger temperature in response acupuncture appear to be most responsive to acupuncture (Ballegaard et al., 1990, 1991). Using a different approach aimed at increasing the number of subject responding to acupuncture, experimental studies are in progress employing inhibition of CCK-8 in the brain to convert EA non-responders to responders (Li M. et al., 2012). This octapeptide is distributed throughout the brain and impairs the action of opioids (Noble et al., 1993; Tang et al., 1997; Zhao, 2008; Heinricher et al., 2001). Thus, CCK-8 may underlie the absence of response to acupuncture in some subjects and antagonism of its action may eventually provide a means to improve responsiveness to EA.

Paradoxical increases in sympathetic activity have been observed during acupuncture. In this regard, a combination of 30 min of bilateral manual acupuncture followed by EA at LI11 and LI4 can elevate pain threshold and MSNA (Knardahl et al., 1998). However, electrical stimulation in this study of pain was at the highest intensity tolerated and involved muscle contraction, so that a muscle sympatho-excitatory reflex response may have elevated rather than reduced the sympathetic response. Furthermore, the control comparison in this study was suboptimal since it involved superficial needle insertion without electrical stimulation, representing a sham procedure that subjects could distinguish from deeper placement of needles accompanied by electrical stimulation.

Another study of unilateral acupuncture applied manually that involved brief stimulation in healthy subjects at LI4, LR3 and SP6 as well as non-acupuncture point stimulation (but not application of a control non-penetrating needle) reduced the increases in blood pressure but not MSNA associated with mental stress during the Stroop colour word test and mental arithmetic (Middlekauff et al., 2001). While acupuncture did not influence resting blood pressure or MSNA, this study found that insertion of needles to record sympathetic activity caused an acupuncture-like effect since blood pressure responses to mental stress were reduced when MSNA was recorded. Thus, the action of acupuncture on the sympathetic efferent response to pain and other forms of stress has not been clearly determined because different paradigms and measurement techniques likely have obscured the neural responses and certainly have made comparisons between studies difficult.

### **Sympathetic responses in heart failure patients**

Sympathetic nerve activity is increased in patients with heart failure, and those with the greatest activation have the most limited life expectancy (Cohn et al., 1984). As discussed later in the section on heart failure, acupuncture has been shown to reduce elevated sympathetic activity in this condition.

### **HYPERTENSION AND HYPOTENSION**

Acupuncture does not influence blood pressure when it is within the normal range in human subjects (Li et al., 2004). Conversely, as noted earlier, experimental studies in animal models and observations in human subjects have shown that EA inhibits sympathetic outflow and reduces blood pressure when they are elevated during excitatory reflex activation. The experimental paradigms include, for example, stimulation of sensory nerves in the visceral organs, for example, the gallbladder with bradykinin (related to inflammatory pain), gastric distension in experimental laboratory preparations and exercise in humans (Li et al., 2002, 2004; Tjen-A-Looi et al., 1998; Vickers, 1998).

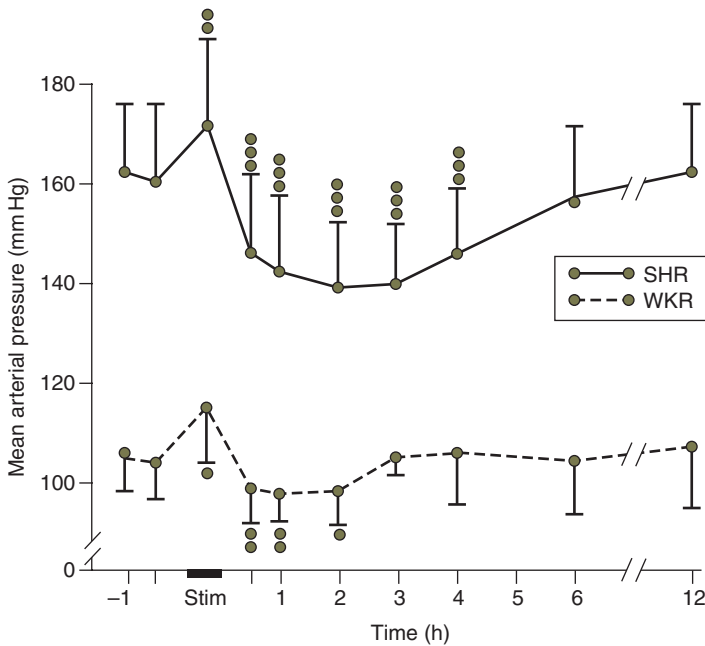
Acupuncture also has an action in hypotension. In this regard, acupuncture has been shown to be capable of reversing hypotension in experimental models of nitroprusside infusion and

haemorrhage (Syuu et al., 2003; Xiao et al., 1983). The influence of acupuncture likewise has been studied during IV infusion of phenylbiguanide (PBG), a 5-HT<sub>3</sub> receptor agonist that stimulates cardiopulmonary vagal afferent endings (Coleridge and Coleridge, 1980; Fu and Longhurst, 1998; Jeggo et al., 2005) to evoke bradycardia and hypotension, simulating the clinical condition of neurogenic or vasovagal syncope, the most common cause of syncope in patients (Calkins and Zipes, 2008; Kapa and Somers, 2008). EA significantly reverses PBG-induced bradycardia and hypotension, in part through actions of opioids and GABA, which modulate vagal preganglionic neuronal activity in the ventrolateral region of the nucleus ambiguus (Tjen-A-Looi et al., 2012). Anatomical studies have shown that preganglionic cholinergic vagal neurons in the nucleus ambiguus that process EA-evoked input are in close proximity to neuronal processes containing enkephalin, further confirming the role of this opioid neurotransmitter in EA modulation of parasympathetic outflow and hypotension (Guo et al., 2012). These data, in aggregate, show that acupuncture has the capacity to normalise blood pressure when it is either transiently increased or decreased experimentally.

Because acupuncture can decrease elevated sympathetic outflow and sympatho-excitatory reflex responses that elevate blood pressure, there is a rationale for using this form of therapy to treat sustained hypertension, particularly forms of hypertension associated with increased sympathetic activity (Longhurst, 2007a,b). However, although TENS and acupuncture in experimental hypertension consistently reduce elevated blood pressure, the results of clinical trials and experimental clinical models of hypertension are mixed.

Both acute and chronic elevations in blood pressure have been examined during acupuncture or TENS. One experimental condition that has been studied during application of TENS is spinal cord injury. Blood pressure can markedly increase (or decrease) during visceral organ stimulation following spinal cord trauma (Cameron et al., 2006). Experimental studies in quadriplegic rats suggest that TENS decreases the exaggerated blood pressure responses associated with colon distension (Collins and DiCarlo, 2002). Although acupuncture appears to be safe as it does not trigger autonomic dysreflexia (Averill et al., 2000), no clinical trials are available on its effect in spinal patients experiencing autonomic dysreflexia. However, chronic elevations in blood pressure in spontaneously hypertensive conscious rats is reduced by acupuncture at ST-36 for periods lasting up to 12 h (Fig. 23.6; Yao et al., 1982).

The SHARP trial (Stop Hypertension with Acupuncture Research Trial), which treated patients with moderate hypertension over a 12 week period, demonstrated no influence on blood pressure over and above the response to an invasive sham control when blood pressure was measured intermittently with mercury sphygmomanometers (Macklin et al., 2006). Other studies have shown a depressor action of acupuncture in clinical hypertension. For example, a small study of 50 patients suggests that 30 min of acupuncture lowers both systolic and diastolic pressure (Chiu et al., 1997). Two other trials, one published in full form and one as a preliminary communication, incorporating ambulatory monitoring to record blood pressure many times throughout the day and frequently at night have demonstrated small but consistent decreases in blood pressure in patients with mild to moderate hypertension (Fig. 23.7; Flachskampf et al., 2007). This hypotensive action of acupuncture appears to be increased by using EA applied for 30 min once weekly to stimulate acupuncture points that have been shown in experimental studies to have a strong cardiovascular influence (PC5, PC6, ST36 and ST37, see Fig. 23.1). In this latter regard, recent investigation suggests that acupuncture in 70–80% of hypertensive individuals influences elevated systolic and mean arterial pressure more than diastolic blood pressure (Li et al., 2015). The onset of acupuncture's hypotensive action appears to be slow, frequently requiring a course of acupuncture treatment over several (2–6) weeks before a sustained decrease in blood pressure is observed. Ambulatory blood pressures decrease by 5–20 mmHg during a course of 6–8 weeks of therapy and tends to remain reduced (relative to pretreatment levels) for up to 4 weeks following cessation of treatment. Although additional studies are needed, the preponderance of evidence suggests

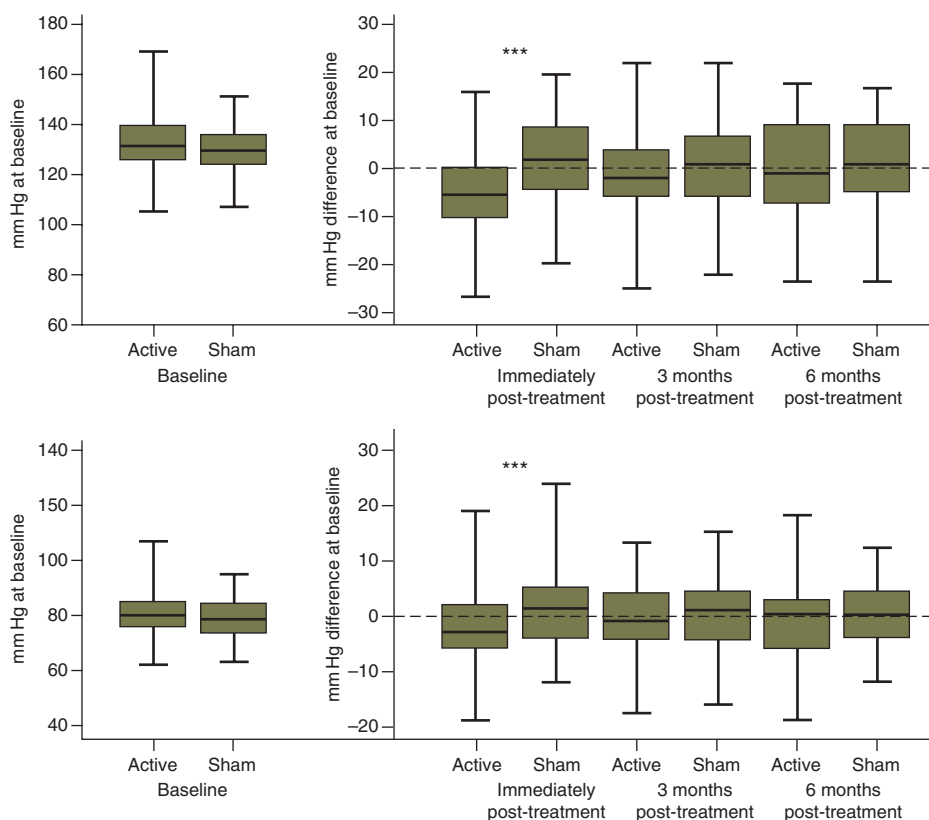


**Figure 23.6** Blood pressure responses to 30 min of 3 Hz sciatic nerve stimulation (as a surrogate for EA) in unanaesthetised spontaneously hypertensive rats (SHR) compared to control Wistar-Kyoto normotensive rats (WKR). The depressor response lasted for up to 12 h in selected animals and significantly (●) for 4 h for the hypertensive group overall. The response was absent in anaesthetised (chloralose-urethane) animals (data not shown). Means and standard deviations are shown. (Reproduced from Yao, T., Andersson, S., Thoren, P., 1982. Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized spontaneously hypertensive rats. *Brain Res.* 240, 77–85, with permission from Elsevier.)

that acupuncture applied repetitively and particularly targeting cardiovascular active acupuncture points can reduce blood pressure in patients with mild to moderate hypertension.

## CHOLESTEROL

In addition to its effect on hypertension, laboratory studies demonstrate that acupuncture can lower diet-induced elevations in cholesterol. Daily brief (ten rotations in 2 s) manual acupuncture at LR3 or 20 min of 18 Hz EA for 20 min at ST40 compared to stimulation of a non-acupuncture point for a 2 week period reduces the increase in cholesterol in experimental models fed high cholesterol diets (Li and Zhang, 2007; Wu and Hsu, 1979). Interestingly, EA at ST40 appears to regulate not only the expression of genes directly involved in the cholesterol metabolism in the liver, but also significantly affects genes involved in signal transduction, transcriptional regulation, cell cycle, cell adhesion, immunity and stress (Li and Zhang, 2007). Although there are no good randomised controlled clinical trials, a small non-randomised, unblinded trial of EA that did not incorporate a control acupuncture point group demonstrated similar or greater weight loss, LDL cholesterol and triglyceride reduction and greater HDL reduction, compared to a control group that were fed a low caloric diet (Cabioglu and Ergene, 2005). More adequately powered, prospective clinical trials incorporating adequate controls need to be conducted to determine if acupuncture effectively lowers cholesterol in patients with or without coronary disease.



**Figure 23.7** Hypotensive response of patients with mild hypertension to an intensive 6 week course of manual acupuncture using pattern diagnosis to select acupuncture points for stimulation. Compared to the sham group, both systolic and diastolic ambulatory blood pressures were lowered significantly (\*\*\*) by acupuncture, a response that was reversed at 3 and 6 months follow-up. Sham acupuncture was performed at acupuncture points selected without relevance to the Chinese hypertension type. Differences between the two groups were 6 and 4 mmHg, for systolic and diastolic blood pressures, respectively. (Reproduced from Flachskampf, F.A., Gallasch, J., Gefeller, O., Gan, J., Mao, J., Pfahlberg, A.B., Wortmann, A., Klinghammer, L., Pflederer, W., Daniel, W.G., 2007. Randomized trial of acupuncture to lower blood pressure. *Circulation* 115, 3121–3129, with permission from the American Heart Association.)

## OBSESITY

Not only is obesity an independent cardiovascular risk factor, but it also leads to development of other risks, including hypertension, hyperglycemia and hypercholesterolemia (Hubert et al., 1983). Stimulation of auricular acupuncture points used to treat overweight patients provides input to regions of the brain that regulate food ingestion, including the ventromedial and ventrolateral hypothalamus (Shiraishi et al., 2009). However, the efficacy of acupuncture to consistently assist with weight loss in obesity is less certain. Experimental studies (Asamoto and Takeshige, 1992) in rats have shown that auricular acupuncture leads to a 5% loss in weight over a period of 2–3 weeks in association with activation of the ventromedial hypothalamus (satiety centre) but not the ventrolateral hypothalamus (feeding centre). The results of clinical trials are mixed, with uncontrolled studies showing small decreases in body weight (Dung, 1986; Huang et al., 1986; Mazzoni et al., 1999; Mok et al., 1976; Sacks, 1975; Shafshak, 1995; Soong, 1975; Sun and Xu, 1993) and many showing either very modest or no weight loss that could be ascribed to

acupuncture. Most trials lack suitable controls, are descriptive and of short duration (<12 weeks) and have used non-standardised treatment protocols employing pattern diagnosis (Lacey et al., 2003). Randomised controlled trials of acupuncture that have resulted in weight loss have documented a positive effect on short-term weight loss, but this response generally has not been observed in the absence of dietary or behavioural interventions. Thus, high quality clinical weight loss trials using acupuncture represent another area of needed research. It will be important to demonstrate an independent effect of acupuncture over and above the influence of standard diet and exercise interventions.

## SMOKING CESSATION

Quitting smoking has an immediate and long-term benefit on coronary risk (Anthonisen et al., 2005; Eliasson et al., 2001; Iso et al., 2005). Because acupuncture leads to the release of endogenous opioids, it has been thought that it may be useful in treating addictive habits like smoking (see Chapter 26). In this regard, acupuncture reduces withdrawal symptoms in subjects addicted to opiates like morphine (Han and Zhang, 1993; Wen and Cheung, 1973). However, meta-analyses of randomised single blinded clinical trials on smoking cessation comparing acupuncture to sham acupuncture indicate no consistent benefit of acupuncture over sham, nor is acupuncture better than no treatment (White et al., 1999, 2011). Furthermore, many trials in this area are low quality as they do not contain testable hypotheses, frequently are short-term, lack suitable controls and do not provide sufficient information to assess their quality (White et al., 1999). Thus, at present, insufficient data are available to determine the efficacy of acupuncture in smoking cessation. More high quality research needs to be conducted in this area.

## Other cardiovascular conditions

### ARRHYTHMIAS

Early experimental studies in a rabbit model using electrical stimulation of the ventromedial hypothalamus to evoke premature ventricular contractions (PVCs), including ventricular tachycardia, demonstrated that low frequency, low intensity EA at PC6 and ST36 reduces extrasystolic potentiation in the absence of a change in blood pressure (Guo et al., 1981). Likewise, reperfusion-related ventricular tachycardia in rats following 3 min of coronary artery occlusion is reduced by EA at PC5 and PC6 in association with a decrease in myocardial oxygen demand, measured as a reduced double product and decreased ST segment elevation (Lujan et al., 2007). A meta-analysis that reviewed 571 potential studies found 10 that met inclusion criteria of randomised controlled single acupuncture intervention trials of cardiac arrhythmias (Kim et al., 2011). Trials in this review evaluated the response of paroxysmal supraventricular tachycardia (PSVT), PVCs or atrial fibrillation to acupuncture. Two studies of PSVT noted similar HR responses as with drug intervention (Dong, 2006; Qi and Zhao, 1993), while a third studying the responses to long-term treatment found similar rates of conversion to sinus rhythm (Wu and Lin, 2006). Three randomised controlled trials of PVCs showed similar responses to acupuncture as with antiarrhythmic medication therapy (Liu, 2005; Yuan and Ai, 2002; Zhong, 2008). Two studies suggested a beneficial effect of acupuncture in conversion from atrial fibrillation to sinus rhythm (Lomuscio et al., 2011; Xu and Zhang, 2007). One of these was a small study of patients with chronic atrial fibrillation, which demonstrated that over a 12 month period acupuncture at PC6, HT7 and BL17 was almost as effective as amiodarone and much more effective than either no therapy or sham acupuncture (needling outside meridians) in preventing reoccurrence of atrial fibrillation after electrical cardioversion (Lomuscio et al., 2011). Kim et al., 2011 concluded that although acupuncture may be effective treatment for arrhythmias, the majority of studies were low

methodological quality and included small sample sizes. Additional high quality studies in this area are warranted.

## PERIPHERAL VASCULAR DISEASE

Blood flow measured by photoplethysmography in normal female subjects is increased in both skin and muscle, specifically in the region of needling (using green and near infrared LED to discriminate superficial and deep flows, respectively), during 20 min of deep but not in response to superficial manual acupuncture at ST36 (Sandberg et al., 2003, 2004). The sensation of *de qi* in this study was elicited by needle manipulation during deep acupuncture. Deep acupuncture (20 mm depth) with or without *de qi* sensation elicits greater increases than superficial acupuncture (2–3 mm, without needle manipulation), but the largest increases within the first 5 min are associated with the acupuncture-induced paraesthesia, suggesting that more aggressive nerve stimulation leads to greater vasodilation. Conversely, superficial needling in female patients with fibromyalgia can result in significant increases in skin and muscle flow (Sandberg et al., 2004). Of note, the local increases in flow measured in Sandberg's studies are likely to represent a local or regional influence of needling (see the succeeding text) rather than a systemic influence, since the responses are rapid (onset in <5 min), whereas acupuncture's systemic cardiovascular actions that are dependent on processing through the long-loop pathway in the brain and resulting changes in sympathetic outflow typically occur 10–15 min after the onset of stimulation (Longhurst, 2010b). Also, as noted earlier acupuncture applied to normal subjects does not alter systemic arterial blood pressure (Li et al., 2004) further arguing against a systemic action of this modality in Sandberg's 2003 study.

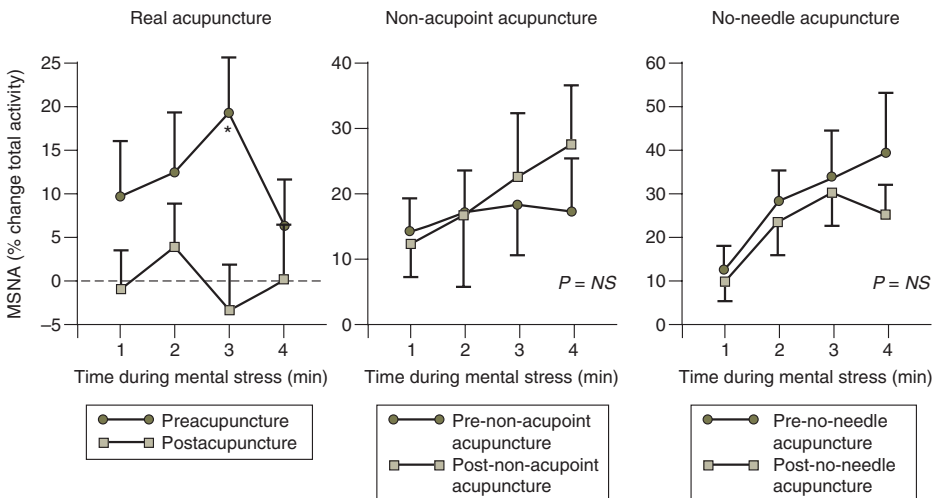
Alternating high with low frequency, high intensity EA (80/2 Hz, 20 mA) applied locally increases survival of ischemic skin flaps and peripheral blood flow in rats either through its local actions on vasodilator mediators or through a sympatho-inhibitory effect (Jansen et al., 1989a,b). Consistent with the former hypothesis as well as with Sandberg's data, a recent study demonstrated that acupuncture may reduce pain by increasing local concentrations of breakdown products of high energy phosphates, including ATP, ADP, AMP and adenosine, which could cause regional vasodilation (Goldman et al., 2010). However, there also is evidence for EA-induced reflex sympatho-inhibition during stimulation using a broad range of intensities (1.5–10 mA) (Noguchi et al., 1999).

Similar to laboratory investigations, a small clinical study employing low frequency high intensity (1–2 Hz, 15–30 mA) TENS in patients with diabetic and non-diabetic (possibly atherosclerotic) peripheral vascular disease showed improvement in toe oxygen saturation, symptoms of claudication and progression of gangrene (Debrececi et al., 1995). High frequency (80 Hz) TENS also increases the survival of skin flaps in experimental models as well as in patients undergoing reconstructive surgery (Kjartansson et al., 1988; Cramp et al., 2002; Lundeborg et al., 1998). Spinal cord stimulation, which may activate many of the same central neural regions as acupuncture (Longhurst, 2001), increases skin temperature, reduces pain, ulcer formation and leads to tissue salvage in patients with peripheral vascular insufficiency (Augustinsson et al., 1985; Jivegard et al., 1987, 1995). No prospective randomised large trials of acupuncture's influence in patients with peripheral vascular disease have been published. Thus, symptomatic peripheral arterial disease represents yet another area where future studies are needed.

## HEART FAILURE

Heart failure is associated with sympathetic overactivity (Hasking et al., 1986; Leimbach et al., 1986), which, in turn, increases cardiac afterload, regional vasoconstriction and diverts blood flow, thus reducing cardiac output and regional organ function (Longhurst et al., 1976) and

ultimately life expectancy of patients (Cohn et al., 1984). Since blockade of the sympathetic activity as first line therapy for patients with advanced heart failure (CIBIS Investigators and Committees, 1986; Hjalmarson et al., 2000; Packer et al., 2002) is associated with serious side effects, there is a rationale for considering acupuncture adjunctive treatment of heart failure to reduce sympathetic outflow. In this respect, a small study comparing 15 min of manual acupuncture (15 s of actual mechanical stimulation) at LI4, LR3 and PC6 versus non-acupuncture point stimulation and no needle stimulation in patients with advanced heart failure documented decreased MSNA during mental stress in response to acupuncture but not during control stimulation (Fig. 23.8; Middlekauff et al., 2002). Resting muscle sympathetic activity in these patients was not altered by acupuncture. Another limited study of eight patients with dilated cardiomyopathy from China (Huang et al., 1986) suggests that a single application of EA at PC6 compared to sham control stimulation increases echocardiographically measured end-diastolic and stroke volumes 1 h later. Recently, a placebo controlled study, employing standardised manual acupuncture at unnamed acupuncture points in 17 heart failure patients (New York Heart Association class II and III) treated twice weekly for 5 weeks, yielded improvement in the 6-min walk distance, postexercise recovery, ventilatory inefficiency and HR variability index (standard deviation of normal to normal R-R intervals over 24h) (Kristen et al., 2010). There was a tendency in this latter study for improvement in the general health and quality of life scores and a small subset of patients demonstrated a decrease in the inflammatory cytokine, tumour necrosis factor alpha. Left ventricular ejection fraction and maximal exercise capacity were unchanged, however. The study is limited by the lack of full description of the acupuncture technique, the small size, lack of long-term follow-up and the use of a non-penetrating sham control (along with the absence of *de qi* in the controls). Additional, larger trials are needed to confirm and extend the results of this interesting investigation.



**Figure 23.8** Attenuation of significant (\*) increase in muscle sympathetic nerve activity (MSNA) by brief manual acupuncture at LI4, LR3 and PC6 in patients with New York Heart Association functional class II and III heart failure. Controls, which included stimulation of non-acupuncture points on the anterior deltoid and non-penetrating tapping of the needle guide on the upper trapezius, did not alter MSNA. Average ejection fraction in these patients was  $23 \pm 3\%$ . (Reproduced from Middlekauff, H., Hui, K., Yu, J., Hamilton, M., Fonarow, G., Moriquichi, J., Maclellan, W., Hage, A., 2002. Acupuncture inhibits sympathetic activation during mental stress in advanced heart failure patients. *J. Card. Fail.* 8, 399–406., with permission from Elsevier.)

## Concluding comments

Experimental studies show that, through stimulation of sensory nerve pathways that project to cardiovascular regulatory regions in the brain and spinal cord, acupuncture has the ability to markedly reduce sympathetic outflow and hence lower elevated blood pressure. Interestingly, acupuncture does not alter blood pressure when it is in the normal range. Studies of acupuncture for patients with mild to moderate hypertension, although variable in design and outcome, largely confirm the results of animal investigations. In addition to lowering blood pressure, acupuncture may be able to reduce demand-induced myocardial ischaemia mainly by lessening demand, rather than increasing the blood supply.

The efficacy of acupuncture in reducing cardiovascular coronary disease risk is much less apparent. It may assist in weight loss, although the changes typically are quite small. It also may reduce elevated cholesterol but does not appear to consistently help patients quit smoking. Clinical trials of acupuncture, however, are not numerous in this field and tend to be small and frequently are not prospective, well-designed, adequately powered or controlled. It is clear that much more research on the role of acupuncture in cardiovascular disease is needed. Both mechanistic studies defining acupuncture's action and prospective, adequately powered and carefully controlled randomised clinical trials should be conducted. Mechanistic studies can help guide the clinical studies by identifying points that can exert the strongest cardiovascular influence, the best modalities of stimulation and the best combinations of acupuncture points stimulated to achieve optimal responses.

A number of issues that often have not been addressed in past studies need to be taken into account in designing new trials for acupuncture. One of the most important considerations in constructing clinical trials of acupuncture is the sham control. The literature suggests that simply placing a needle in an active acupuncture point or stimulation of an 'inactive' acupuncture point may serve as adequate 'strong' controls (Mayer, 2000; Zhou et al., 2005), since in the absence of neural stimulation (i.e. stimulation outside a classical meridian) *de qi*, the neurological sensation associated with good responses during acupuncture may not occur. Acupuncture trials cannot reliably be double blinded since it is not possible to prevent the acupuncturist from knowing exactly where to place the needle. Blinding of the patient and investigators performing data analysis, however, should occur.

Another issue to consider in constructing acupuncture trials is the method for choosing acupuncture points. On one hand, TCM theory dictates that acupuncture points should be selected after obtaining a history followed by tongue and pulse physical diagnosis. This traditional method of pattern diagnosis leads to selection of variable combinations of points that are stimulated, depending on the individual acupuncturist's assessment. The different locations of stimulation likely increase the number of patients that have to be included to adequately power studies and thus determine statistically significant responses to acupuncture. This approach has led to more failures than successes in studies addressing clinically significant cardiovascular responses to acupuncture.

A more standardised approach, commonly adapted in Western medical acupuncture trials, is to select a fixed number of points that are always stimulated. Observations in experimental studies can help guide in the selection of the best points to stimulate to evoke reproducible acupuncture-cardiovascular responses (Li et al., 2015). This standardised approach guided by modern biology may seem repugnant to many TCM practitioners, but it does allow critical testing of acupuncture's clinical responses in smaller numbers of subjects.

## Clinical application of acupuncture

Acupuncture likely can be used safely to treat patients with mild to moderate hypertension, that is, blood pressures below 170/105 mm Hg. Approximately 70% of patients will respond to the intervention, but unfortunately at the present time, we cannot reliably determine which patients

are more likely to be responsive. It should be kept in mind that acupuncture, especially EA, is most effect in reducing systolic and mean blood pressure and is less effective in reducing diastolic pressure. Hence it may be useful in patients with reduced vascular compliance, including older patients. It can be used in patients off pharmacological therapy or in combination with antihypertensive drugs, but only after approval of the patient's primary care physician. Practitioners should be aware that the onset of action of the blood pressure lowering effects of acupuncture may take several weeks, if it is employed once weekly for 30 min, using low frequency (2 Hz), low intensity (2–4 mA) EA at those acupuncture points so far shown to display cardiovascular activity, for example, PC5, PC6, ST36 and ST37. Few data are available to guide its use chronically after intensive treatment for 6–8 weeks. Reinforcement of the initial therapy will most likely be required, either once each week or once every other week.

## Future research

A number of important clinical issues still need to be addressed in studies of acupuncture's role in cardiovascular medicine.

1. We need properly constructed clinical trials on smoking cessation, weight loss and cholesterol reduction.
2. The potential for acupuncture to elevate low blood pressure in subjects who have symptomatic hypotension needs to be evaluated since experimental results show that acupuncture increases blood pressure when it has been lowered. The concept in these studies is that acupuncture doesn't just lower elevated blood pressure but rather normalises it by raising it when it is low, lowering it when it is high and not altering it within the normal range.
3. The importance of simultaneously stimulating multiple points, although commonly used by most acupuncturists, has not been evaluated prospectively in trials incorporating sufficiently large sample sizes to provide a definitive answer. Experimental evidence suggests that stronger effects may not be achieved by simultaneously stimulating two strong sets of cardiovascular acupuncture points (Zhou et al., 2005). However, there is evidence that acupuncture can influence multiple regions in the brain, spinal cord and locally in the vicinity of acupuncture needles, which could lead to larger cardiovascular responses if multiple sites are stimulated (Li and Longhurst, 2010). Thus, the regional cardiovascular influence of acupuncture in the spinal cord (Zhou et al., 2006) potentially could be supplemented by its more global actions in higher centres in the hypothalamus, midbrain and medulla as well as its local action at the site of needling (Longhurst, 2007a,b).
4. The question of why only 70% of individuals respond to acupuncture, even when needles are carefully placed in acupuncture points known to have strong cardiovascular effects needs additional study (Li et al., 2004). The counter-regulatory neurotransmitter system cholecystokinin may antagonise the action of opioid neuromodulators that are released by acupuncture during its action on cardiovascular centres in the brain (Huang et al., 2007; Tang et al., 1997). Therefore, administration of an inhibitor of the CCK<sub>A</sub> or CCK<sub>B</sub> receptor system may convert some non-responders into responders or may enhance the effect of acupuncture in responsive individuals.
5. The method of acupuncture application needs further consideration. As noted earlier, TENS causes many of the same cardiovascular responses that occur with acupuncture. TENS helps control pain much like acupuncture (Longhurst, 1998). Although there are fundamental differences between acupuncture and TENS as it is commonly practised (see the preceding text), a non invasive skin electrode system with stimulation parameters that are more like EA (i.e. low intensity and low frequency) could be developed for use in patients who, after seeing an acupuncturist for evaluation and an initial course of therapy, want to take their own responsibility for their long-term health care.

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# Acupuncture for neurological conditions

D.J. Grant

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The knowledge base supporting the use of acupuncture for disorders of the central nervous system has expanded rapidly in recent years, culminating in the endorsement by NICE ([National Institute for Health and Clinical Excellence, 2012](#)) of acupuncture as a treatment for chronic tension-type headache and chronic migraine. This chapter will also detail the use of acupuncture for stroke, and consider epilepsy, spinal cord injury, multiple sclerosis and neurodegenerative disorders.

## Stroke

### INTRODUCTION

Stroke is the third commonest cause of death in the United Kingdom and the commonest cause of disability in the Western world, costing the economy an estimated £8 billion per year in England alone ([National Audit Office, 2010](#)). Any treatment that could potentially promote motor recovery, reduce disability and prevent institutionalisation and death after stroke would be of great benefit to society.

Historically, acupuncture has been widely used in China for this purpose, with anecdotal reports of significant instantaneous effects in acute stroke. In Chinese county-level hospitals, where Western-style stroke rehabilitation is relatively under-developed, acupuncture is the main complementary

therapy used for stroke, and it is also still used in around half of patients in higher level university hospitals (Zhang et al., 2009). The acupuncture technique used is highly variable and in part depends upon the Traditional Chinese Medicine (TCM) diagnosis, with electroacupuncture (EA) being used in most patients. The relatively new technique of scalp acupuncture developed in China in the 1970s is also frequently used (Liu et al., 2012). In this paradigm, points on 14 scalp acupuncture lines similar to meridians on the body are used to stimulate specific areas of the cerebral cortex; needles are inserted into the subcutaneous tissue at a relatively shallow angle and generally stimulated rapidly in bursts of a few minutes. A similar system is also in use in Japan (Yamamoto, 1989).

In the last 2 decades there has been a growth of interest in the Western world in exploring the use of acupuncture in stroke rehabilitation, though the results of this endeavour have been mixed.

## EVIDENCE FROM CLINICAL TRIALS

The resurgence of interest in acupuncture for stroke was sparked by Barbro Johansson's group in Sweden. Building on evidence from animal models of stroke that sensory stimulation can modify neuronal connections and cortical maps, and emerging evidence from neuroimaging studies using positron emission tomography (PET) that functional reorganisation in the brain occurs after stroke (Chollet et al., 1991; Weiller et al., 1992), she sought to ask whether acupuncture as a form of sensory stimulation could improve functional outcomes in stroke patients. In a seminal paper, Johansson et al. (1993) randomised 78 patients within 10 days of acute stroke to conventional stroke rehabilitation alone or rehabilitation plus acupuncture. Acupuncture was given for 30 min twice weekly for 10 weeks, using a combination of traditional acupuncture points including LI4, LI11, ST36, ST40, GB34, TE5 bilaterally, GV20 and three extra points on the hemiparetic side. Manual stimulation was used to achieve *de qi* and was combined with low-frequency EA at 2–5 HZ between two arm and two leg points on the affected side (K. Johansson, personal communication). The results of this trial were striking. At 3 months poststroke, patients in the acupuncture group showed highly significant improvements in activities of daily living, as measured by the Barthel index, and in quality of life: scores improved in four of the six domains of the Nottingham Health Profile (energy, mobility, emotion and social isolation). Most of these improvements were maintained at 12 months, and even more significantly, 25 out of 28 of the surviving patients were living at home, compared with 21 out of 32 patients in the control group, with the shorter duration of institutionalisation resulting in a mean cost saving of \$26 000 per patient (1993 value). Similar significant long-term functional improvements were shown by Kjendahl et al. (1997).

Sadly, the therapeutic optimism generated by these results largely faded as further experimental evidence accrued (Gosman-Hedstrom et al., 1998; Johansson et al., 2001). However, in interpreting the later evidence one should bear in mind a number of factors. Firstly, the publication of this trial coincided with a massive upturn in the provision of stroke services in many Western countries, fuelled by the realisation that organised care in dedicated Stroke Units saves lives and improves outcomes (Dennis and Langhorne, 1995). Hence it is more of a challenge to show in a pragmatic trial that acupuncture (or any other physical treatment) has an additional benefit over and above standard stroke rehabilitation. Secondly, stroke trials have used a variety of outcome measures and whilst ultimately the most relevant, and the most easily measurable may be 'death or dependency' (Dennis et al., 1997), this may be too blunt an instrument with which to identify subtle improvements in mobility or function that may still be of benefit to the patient.

For example, in the study of Park et al. (2005) in patients with subacute stroke, acupuncture was no better than sham acupuncture using a blunt, telescopic, non-penetrating needle (the Park sham device) on the primary outcome measure of performance of activities of daily living (Barthel index). But in a post-hoc analysis, a subgroup of more severely affected patients showed a significant improvement in leg function. A similar observation was made by Alexander et al. (2004) in a similar patient group: compared to standard stroke rehabilitation, acupuncture showed no benefit in overall motor recovery but a definite benefit in lower limb function.

## SYSTEMATIC REVIEWS

In recent years six systematic reviews have been published on acupuncture and stroke and I will review them briefly. [Park et al. \(2001\)](#) reviewed all randomised controlled trials of acupuncture as a treatment for stroke published to date. Nine trials (538 patients) were included. Six trials were 'positive' and three 'negative', however only two trials were of adequate methodological quality and these were both negative. Because of the heterogeneity of outcome measures used in the individual trials it was not possible to perform a formal meta-analysis.

[Sze et al. \(2002\)](#) did manage to perform a rigorous meta-analysis of published trials, unearthing more from the Chinese literature. They were careful to include patients within 6 months of the onset of stroke, and to include trials with internationally recognised (or, in the case of China, nationally recognised) outcome measures, and to separate out trials in which the participants additionally received 'stroke rehabilitation' from those in which they received 'conventional care' only. In total 14 trials with 1213 patients were included. For the comparison of acupuncture versus no acupuncture in addition to 'stroke rehabilitation', there was no significant improvement in motor impairment but a small positive effect on disability, amounting to approximately 2.6 points on the Barthel index. However, in a subgroup analysis, this positive effect on disability was only seen in studies with inadequate randomisation or without assessor blinding. Furthermore, in three trials comparing acupuncture with a sham technique, there was no significant difference in motor recovery or disability. In a separate analysis, in trials in which the additional treatment was 'conventional care' (i.e. not formal stroke rehabilitation), acupuncture had a clear positive effect on disability. But one should note that such trials will never again be performed and that their conclusion is of doubtful relevance to modern Western stroke medicine.

There are two systematic reviews in the Cochrane Library. [Zhang et al. \(2005\)](#) studied acupuncture for acute stroke, specifically restricting their analysis to patients recruited within 30 days of stroke onset. Fourteen trials with a total of 1208 patients were included, and compared to the work of Sze et al., five additional trials were included, four from China and one unpublished trial from the United Kingdom. The overall conclusion was that there was no benefit of acupuncture in acute stroke, but that patient numbers were too small to draw a definitive conclusion. Hidden in this negative conclusion, one might note significantly fewer patients being dead or needing institutional care, but this is based on the results of only one unpublished report and two published trials ([Gosman-Hedstrom et al., 1998](#); [Johansson et al., 1993](#)). [Wu et al. \(2006\)](#) attempted to evaluate the efficacy of acupuncture for subacute or chronic stroke, that is, for patients recruited at least 1 month after the event. Five trials (368 patients) met the inclusion criteria but methodological quality was inadequate to draw any conclusions.

More recently, [Kong et al. \(2010\)](#) performed a meta-analysis of acupuncture for functional recovery after stroke (any duration), focussing on the comparison between acupuncture and sham acupuncture and aiming to include all relevant trials, particularly those from Japan and Korea that may have been missed by previous authors. Ten trials with a total of 711 patients were included. Once again, there was no positive effect of acupuncture on functional recovery (i.e. no reduction of disability). In contrast, [Wu et al. \(2010\)](#) used rather broad inclusion criteria to systematically review 'acupuncture in poststroke rehabilitation' and identified 56 trials, 35 Chinese and 21 Western, of which 23 had a publication date of 2006 or later, that is, were subsequent to the Cochrane reviews. A variety of techniques were used, including EA in 16, body and scalp acupuncture in 24 and scalp acupuncture only in 4. Thirty-eight of these trials provided sufficient data for inclusion in the meta-analysis. The results were strongly in favour of acupuncture, prompting the conclusion that acupuncture may be effective in poststroke rehabilitation, but once again poor study quality and the possibility of publication bias hindered the strength of this recommendation. The authors conducted a metaregression analysis in order to tease out if specific factors contributed to the heterogeneity observed between the studies: indeed country of origin (China vs. elsewhere), the use of manual versus EA, the use of sham controls versus no use of sham in the control group and

the adequate reporting of randomization all contributed significantly to heterogeneity and may have affected the results. It is worth noting that this analysis does provide some evidence for the superiority of EA over manual acupuncture in stroke rehabilitation.

## SPASTICITY

Acupuncture may also have benefits on spasticity. [Zhao et al. \(2009\)](#) studied a Chinese population of chronic stroke patients and compared two groups, one receiving 'traditional acupuncture' (PC6, SP6, GV26, HT1, LU5, BL40 and GB20) and one receiving additionally scalp acupuncture targeted at the hypothetical 'surface projection zone of the decussation of the pyramids' (four points on the cranium in the region between BL9 and BL10). Both groups showed significant improvements in both upper and lower limb spasticity clinically and electromyographically, with the second group responding better. Similarly [Yan and Hui-Chan \(2009\)](#) showed that TENS applied for 60 min five times a week for 3 weeks to acupuncture points ST36, LR3, GB34 and BL60 in acute stroke patients reduced ankle spasticity and increased dorsiflexor strength, compared to both placebo TENS and stroke rehabilitation alone.

## DYSPHAGIA

Acupuncture is widely used in China to treat dysphagia in acute stroke and [Xie et al. \(2008\)](#) attempted a meta-analysis on this subject for the Cochrane Library. They searched for trials in which patients were recruited within 30 days of stroke but were only able to identify one Chinese trial, that of [Han \(2004\)](#). Sixty-six patients with dysphagia following acute stroke were studied. Twelve out of thirty-four patients (35%) treated with acupuncture in addition to standard Western medical treatment and nasogastric feeding recovered to normal feeding compared with 7 out of 32 in the control group (22%). This difference was not significant and, not surprisingly, no conclusion could be drawn from the systematic review. However, one promising trial was awaiting assessment at the time of the review. [Seki et al. \(2005\)](#) recruited 32 patients with poststroke dysphagia and randomised them to receive acupuncture at ST36 and KI3 three times a week for 4 weeks or conventional care. Videofluoroscopy was performed by a blinded radiologist before and after treatment, and significant reductions in aspiration of water and pharyngeal retention of both water and food were demonstrated in the acupuncture group.

More recently, [Long and Wu \(2012\)](#) performed a further meta-analysis of acupuncture for poststroke dysphagia, not confining the analysis to acute stroke patients. They identified 72 randomised controlled trials from the Chinese literature, in which the comparison was between routine treatment (including rehabilitation) and routine treatment plus acupuncture. Overall there was a highly significant treatment effect in favour of acupuncture, and although the study quality was generally very poor, the positive result was robust in a subgroup analysis of the four higher-quality studies. The use of acupuncture for dysphagia in stroke patients certainly seems worthy of further study.

## MECHANISM OF ACTION

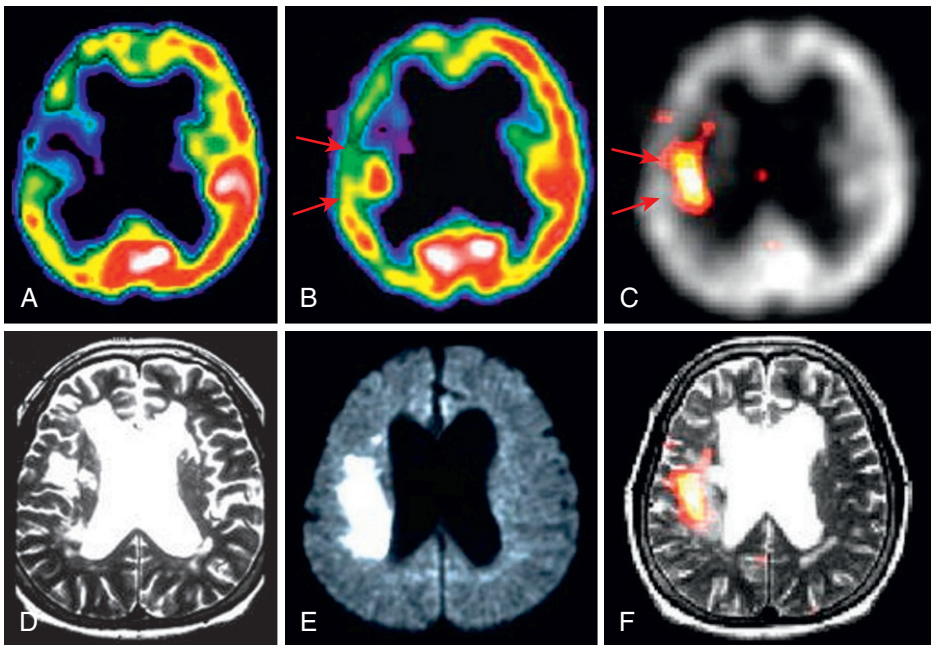
If acupuncture were to be of physiological benefit in stroke patients, what might be the mechanism? There is a growing body of evidence from studies using PET and functional MRI (fMRI) that recovery from stroke is associated with functional reorganisation within the brain, and that this neuronal plasticity can be enhanced by an enriched sensory environment and a variety of physical treatments ([Johansson, 2000](#)). There is now radiological evidence that acupuncture too can affect cortical activation and thereby potentially enhance neuronal plasticity. [Schaechter et al. \(2007\)](#) performed fMRI studies in seven stroke patients undergoing manual and EA (four

patients) or sham acupuncture (three patients), the treatment being based on TCM principles. They showed a highly significant positive correlation between changes in function of the affected arm and activation in the contralateral motor cortex, though within this very small study it was not possible to conclude that verum acupuncture was more effective than sham. And similarly a small fMRI study by [Chau et al. \(2010\)](#) suggested a correlation between dysphasia scores and activation in Wernicke's area in seven dysphasic stroke patients treated with acupuncture.

A similar and related hypothesis is that acupuncture stimulates blood flow in the ischaemic brain. [Lee et al. \(2003\)](#) studied six young patients with dense strokes and measured changes in regional cerebral blood flow using single-photon emission computed tomography (SPECT) with MRI coregistration. Manual acupuncture was performed at traditional acupuncture points (LI4, LI10, LI11, LI15, LI16 and TE5) on the affected arm of the patients. All patients showed focally increased cerebral blood flow in the periphery of the ischaemic area, or in the hypoperfused zone in the affected vascular territory ([Fig. 24.1](#)). This suggests that acupuncture may be activating viable tissue and enhancing metabolic activity in the ischaemic penumbra.

These emerging radiological findings may in turn stimulate further clinical studies in this field.

Evidence from animal studies is now also emerging to show that acupuncture (EA in particular) can convey neuroprotection by inhibiting apoptotic cell death. In an animal model of



**Figure 24.1** (A–F) Increased regional cerebral blood flow (rCBF) in the ischaemic zone after acupuncture. (A) Baseline perfusion single-photon emission computed tomography (SPECT) obtained 3 weeks after symptom onset in a patient with right middle cerebral artery (MCA) occlusion shows perfusion defect in right frontal lobe with surrounding hypoperfusion. (B) SPECT 8 days later shows acupuncture-induced increased rCBF in the hypoperfused zone (arrows). (C) Subtraction of the baseline and postacupuncture image shows this more clearly (arrows). (D, E): T2- and diffusion weighted MRI (DWI): the area giving normal signal in D high signal intensity in E is taken to represent cytotoxic oedema within the viable ischaemic zone. (F) Superimposition of C and D: acupuncture-induced increase in rCBF occurred in the peri-infarct ischaemic zone. (Reproduced from Lee, J.D. et al., 2003. *The cerebrovascular response to traditional acupuncture after stroke*. *Neuroradiology* 45, 780–784. Figure 1, © Springer-Verlag 2003, with kind permission from Springer Science + Business Media.)

ischaemic brain injury, [Zhou et al. \(2011\)](#) subjected experimental rats to middle cerebral artery occlusion, and showed that EA at points GV20 and GV26 commencing five minutes after the brain injury reduced the size of the infarct, neurological deficit and death rate, and improved cerebral blood flow measured by Doppler. They also showed that the parameters of EA were important, with an amplitude of 1.0–1.2 mA and frequency of 5–20 Hz being essential for therapeutic benefit. Then in a further experiment ([Zhou et al., 2013](#)), this group also demonstrated that the duration of EA was crucial. Thirty minutes of EA significantly reduced infarct volume, attenuated neurological deficit and reduced death rate, but surprisingly, when EA was given for 45 min, the results were the opposite: neurological deficits and infarct volume were not reduced and death rate was increased, and this despite the fact that cerebral blood flow was still increased by treatment.

This work suggests that the mechanisms by which EA causes neuroprotection are more complex than simply improving cerebral blood flow. In this study, the neuroprotection induced by the optimal period of EA (30 min) was almost completely blocked by the intravenous injection of naltrindole, an antagonist of the  $\delta$ -opioid receptor (DOR). There is evidence that stimulation of the DOR is important in attenuating hypoxic, ischaemic or excitatory brain injury, and that DOR activation is associated with promotion of pro-survival neurotrophic signalling and inhibition of apoptotic signalling ([Chen et al., 2014](#)). DOR activation may therefore be one mechanism by which an appropriate EA stimulus achieves neuroprotection. However it is likely that many other neurotransmitters including glutamate, GABA, monoamines and cannabinoids are also involved ([Li X et al., 2012](#)).

Further evidence on the mechanism by which EA causes neuroprotection comes from an animal model of traumatic brain injury ([Chuang et al., 2013](#)). Rats were subjected to brain injury by fluid percussion and then treated immediately with low-frequency EA at GV20, GV26, LI4 and KI1 for 30 or 60 min. EA for 60 min in this model significantly increased regional blood flow, reduced infarction volume and improved motor function, and also reduced the number of apoptotic cells and the expression of transforming growth-interacting factor, an important factor in the signalling pathway of cell apoptosis.

Similar findings are emerging from research in ophthalmology (see [Chapter 30](#)) in which glaucomatous optic neuropathy appears to take place through apoptosis of the retinal ganglion cells, mediated by neurotrophins such as nerve growth factor and brain-derived neurotrophic factor which can be modulated by acupuncture ([Rom, 2013](#)).

## SUMMARY

The present state of the evidence suggests that the addition of acupuncture to conventional stroke rehabilitation is unlikely to be of benefit when this is measured using broad global outcomes such as improvement in overall motor function, reduction in disability, improvement in quality of life or reduction in death or institutionalisation. More subtle benefits, particularly on lower limb function and spasticity, may be worthy of further exploration. Experimental work suggests that optimising the parameters of EA may be crucial to achieving a therapeutic benefit. In animal models, evidence is emerging that EA can cause neuroprotection by modulating neurotrophins and inhibiting apoptotic cell death.

## Headache

### INTRODUCTION

Headache is one of the most frequent symptoms presenting to general practitioners and neurologists. The differential diagnosis of chronic headache includes tension-type headache, migraine, cluster headache, trigeminal neuralgia and rarer forms of benign paroxysmal headache ([International Headache Society, 2004](#)), with sinister causes being uncommon.

The typical description of tension-type headache is of a constant generalised bilateral headache which may continue for days or even weeks, with a pressing or tightening quality, of mild to moderate intensity and not aggravated by routine physical activity. The International Headache Society (IHS) further subdivides tension-type headache into 'episodic' and 'chronic' forms, based mainly on number of headache days per month. Acupuncture researchers have tended to include both subgroups in clinical trials, though it is conceivable that they might respond differently to treatment. In contrast, migraine is typically experienced as a severe, disabling, paroxysmal, unilateral, pulsating headache, associated with nausea, vomiting or photophobia and, in 'classical' migraine, an 'aura' or focal neurological event.

The pathogenesis of both common types of headache is still poorly understood. Most intracranial structures (with the exception of the dura and some blood vessels) are insensitive to stimuli which are normally painful and hence the origins of tension-type headache are probably extracranial. Stress is frequently a precipitant and a search for myofascial trigger points in muscles of the neck and shoulders is often rewarding, together with treatment in the region of GB20 at the base of the occiput.

The headache of migraine is thought to be primarily due to vasodilatation of extracranial blood vessels whilst the preceding aura is due to intracranial vasoconstriction. Whilst there are many potential triggers to the migraine attack, there is some evidence that a final common pathway is reduced activity in serotonergic projections, hence the therapeutic use of serotonergic agonists such as triptans to abort the attack. Prophylactic drug treatment for migraine remains unsatisfactory, however, and given the disabling effect of the condition and its impact on quality of life, many sufferers have turned to acupuncture. Treatment regimes generally include local points in the head and neck, particularly GB20 at the occiput and GV20 on the vertex, and distal points, particularly on the foot. The large body of empirical evidence acquired by the leading British acupuncturist Felix Mann pointed to the benefit of treating migraine by needling the region of LR3 on the dorsum of the foot (Mann, 1992).

## EVIDENCE

There is now a body of high quality experimental evidence on acupuncture for headache, thanks to the 'Modellvorhaben Akupunktur', a series of large trials conducted in Germany to determine the efficacy and cost-effectiveness of acupuncture for a variety of chronic conditions. Six of these trials are relevant to this discussion, namely the two acupuncture randomised trials (ART) for migraine and tension-type headache, a comparative trial (COMP) of acupuncture versus metoprolol for migraine prevention the two German acupuncture trials (GERAC) for migraine and tension-type headache, and the Acupuncture in Routine Care (ARC) study for chronic headache. They are summarised in Table 24.1.

The ART trial for tension-type headache (Melchart et al., 2005) recruited patients with episodic or chronic tension-type headache and randomised them to one of three groups: true acupuncture, minimal acupuncture, or waiting list control, in a ratio of 2:1:1. In the true acupuncture group, experienced acupuncturists delivered a semi-standardised treatment consisting of basic points GB20, GB21 and LR3 and optional additional points, in some cases based on TCM diagnosis. Twelve treatments were given over 8 weeks. Those in the minimal acupuncture group received needling to 5 out of 10 predefined 'non-acupuncture points', superficially and avoiding *de qi*. On the primary outcome measure of 'number of days with headache' at 12 weeks, the mean reduction was 7.2 days in the acupuncture group, 6.6 days in the minimal acupuncture group and 1.5 days in the waiting list group. Defining responders in the traditional manner recommended by the IHS as those with at least a 50% reduction in headache days, the response rates were 46% for acupuncture, 35% for minimal acupuncture and 4% for waiting list. Results for secondary outcome measures including disability and quality of life were very similar. The benefits were maintained at 24 weeks.

TABLE 24.1 ■ Summary of the ‘Modellvorhaben Akupunktur’ Clinical Trials for Headache

Trial	Number of Subjects	Treatment	Principal Outcome Measure	Results	Conclusion
ART tension-type headache <a href="#">Melchart et al. (2005)</a>	Ac 132 Minimal Ac 63 Waiting list 75	Semi-standardised 12 treatments over 8 weeks	Reduction in headache days at 12 weeks	Ac $7.2 \pm 6.5$ Minimal $6.6 \pm 6.0$ Waiting list $1.5 \pm 3.7$	Ac vs. waiting list $p < 0.001$ Ac vs. minimal NS
ART migraine <a href="#">Linde et al. (2005)</a>	Ac 145 Minimal Ac 81 Waiting list 76	Semi-standardised 12 treatments over 8 weeks	Reduction in migraine days at 12 weeks	Ac $2.2 \pm 2.7$ Minimal $2.2 \pm 2.7$ Waiting list $0.8 \pm 2.0$	Ac vs. waiting list $p < 0.001$ Ac vs. minimal NS
COMP migraine <a href="#">Streng et al. (2006)</a>	Ac 59 Metoprolol 55	Non-standardised 8–15 treatments over 12 weeks	Reduction in migraine days at 12 weeks	Ac $2.5 \pm 2.9$ Metoprolol $2.2 \pm 2.7$	Ac vs. metoprolol NS
GERAC tension-type headache <a href="#">Endres et al. (2007)</a>	Ac 209 Sham 200	Semi-standardised 10 treatments over 6 weeks (option of further 5)	Proportion of responders (>50% reduction in headache days) at 6 months	Ac 33% <sup>a</sup> Sham 27% <sup>a</sup>	Ac vs. sham NS
GERAC migraine <a href="#">Diener et al. (2006)</a>	Ac 290 Sham Ac 317 Standard care (medication) 187	Semi-standardised 10 treatments over 6 weeks (option of further 5)	Reduction in migraine days at 6 months	Ac $2.3 \pm 3.6$ Sham $1.5 \pm 3.8$ Standard $2.1 \pm 4.0$	NS between groups (Ac vs. Sham $p = 0.017$ in per-protocol analysis)
ARC headache <a href="#">Jena et al. (2008)</a>	Ac 1613 Control 1569 Non-randomised cohort 11874	Non-standardised 15 treatments over 3 months	Number of headache days at 3 months vs. baseline	Ac $4.7 \pm 5.6$ vs. $8.4 \pm 7.2$ <sup>b</sup> Control $7.5 \pm 6.3$ vs. $8.1 \pm 6.8$ <sup>b</sup>	Ac vs. control $p < 0.001$

Ac, acupuncture. Results are mean  $\pm$  SD except for GERAC tension-type headache trial (% responders) and except where stated.

<sup>a</sup>All minor protocol violations resulted in subjects being classified as non-responders.

<sup>b</sup>Results are mean  $\pm$  SE.

The ART trial for migraine (Linde et al., 2005) used an essentially identical design. The semi-standardised treatment in the acupuncture group consisted of basic points GB20, GB40 or 41 or 42, GV20, LR3, TE3 or 5, extra point *Taiyang* and optional additional points. Treatment in the minimal acupuncture group was as in the ART tension-type headache trial. Results were remarkably similar: mean reduction in headache days was 2.2 in both the acupuncture group and minimal acupuncture group and 0.8 in the waiting list group, proportion of 'responders' was 51% for acupuncture, 53% for minimal acupuncture and 15% for waiting list, and benefits were maintained at follow-up.

Overall, the results of both trials showed that acupuncture had a significant and clinically relevant benefit compared to no treatment ( $p < 0.001$ ), but that acupuncture was not significantly better than minimal acupuncture. This raises again the question of the physiological inertness of minimal acupuncture and its validity as a 'sham' intervention in acupuncture trials. The alternative explanation is that all the effects of acupuncture in the context of these trials are due to 'placebo' (i.e. expectation) effects. This is possible, but the magnitude of the effect of minimal acupuncture observed here seems greater than that normally ascribed to placebos in clinical trials (Hrobjartsson and Gotzsche, 2001; Kaptchuk et al., 2006).

The same group also attempted a comparative trial of acupuncture versus metoprolol for migraine prevention (Streng et al., 2006). The acupuncture treatment was non-standardised: the same basic points as in the ART migraine were recommended but the acupuncturist was free to tailor treatment to the individual patient. Between 8 and 15 treatments were delivered over a 12 week period. The metoprolol treatment was 100–200 mg once daily for 12 weeks. The number of migraine days decreased by 2.5 days in the acupuncture group compared to 2.2 days in the metoprolol group, and response rates were 61% for acupuncture and 49% for metoprolol. Acupuncture caused fewer side effects than metoprolol. So the results of this trial support the null hypothesis that acupuncture is as effective and safe as metoprolol, in conditions similar to routine practise. However, several caveats have to be attached to this conclusion. The study was underpowered: recruitment target of 480 patients could not be met, only 114 were randomised, and 31% of patients in the metoprolol group withdrew or were lost to follow-up. Further, about half of those recruited had had previous experience of acupuncture and therefore would have been likely to have a high expectation of success; the primary outcome measure (number of days with migraine) was self-reported and the study unblinded.

The GERAC trial for tension-type headache (Endres et al., 2007) was intended to be a three-arm comparative trial of true acupuncture, 'sham' acupuncture and standard care. However, the 'standard care' treatment was amitriptyline, and recruitment into this arm proved impossible so was quickly abandoned. The acupuncture treatment consisted of obligatory points GV20, LI4, LR 3 or 2 and GB20 or BL10, plus additional points determined by TCM diagnosis. The sham treatment used points outside the classical meridians and not on the head, with shallower insertion of needles and no manual stimulation. Ten treatments were given over a 6 week period, with the option of a further five treatments for partial responders. The results of this trial have been the subject of some debate. The primary outcome measure was the proportion of responders (those with a reduction in number of headache days of greater than 50%), however any minor variation in protocol, including any change of analgesics, even change to a lower strength analgesic, resulted in the patient being classified as a non-responder. On this basis, the response rates were 33% for true acupuncture and 27% for sham ( $p = 0.18$ ). However, using the accepted IHS definition of response as reduction in headache days of greater than 50%, regardless of medication use, response rates were 66% for true acupuncture and 55% for sham, a statistically significant difference ( $p = 0.024$ ).

The GERAC trial for migraine (Diener et al., 2006) was of similar design; 960 patients were randomised in equal numbers to true acupuncture, 'sham' acupuncture or standard care, this being treatment with beta-blockers, flunarizine (a drug not licenced in the United Kingdom) or valproic acid. True and sham acupuncture treatments were as in the tension-type headache trial. For the primary outcome measure, the mean reduction of headache days at 6 months was 2.3 days for

true acupuncture, 1.5 days for sham acupuncture and 2.1 days for standard treatment. The difference between groups was not significant ( $p=0.09$ ), though all groups improved from baseline. However, in a 'per-protocol' analysis, the mean reductions were 2.3 days for true acupuncture, 1.3 days for sham acupuncture and 2.7 days for standard treatment, noting that the number of patients in this group is particularly small (83 out of 308 randomised). In this analysis, the difference between groups is significant ( $p=0.031$ ), as is the difference between true and sham acupuncture ( $p=0.017$ ).

The ARC trial (Jena et al., 2008) was a very large pragmatic trial, in which 3182 patients with chronic headache (including those with both migraine and tension-type headache) were randomised either to receive 15 sessions of acupuncture over 3 months, or to wait 3 months before receiving the same treatment. Those who declined to be randomised were followed up as a non-randomised cohort of 11 874 patients. The acupuncture treatment was entirely non-standardised: physicians were free to choose any number and combination of points but only manual acupuncture was allowed. At 3 months, there was a highly significant difference in number of headache days between the acupuncture group and the control group ( $p<0.001$ ), with highly significant differences also in intensity of pain and quality of life. The benefits of acupuncture were maintained at 6 months, and the benefits seen in the non-randomised cohort were similar.

In an associated cost-effectiveness analysis (Witt et al., 2008), the incremental cost-effectiveness ratio of acupuncture was €11 657 per QALY, which would imply that acupuncture for headache is a cost-effective intervention on internationally accepted criteria.

A similar though somewhat smaller pragmatic trial conducted in a UK General Practice population of patients with chronic headache (Vickers et al., 2004) also showed highly significant benefits of acupuncture (up to 12 treatments over 3 months) versus routine care at 12 months. Results of a cost-effectiveness analysis were also similar, with an estimated cost per QALY of £9180 (Wonderling et al., 2004).

## SYSTEMATIC REVIEWS

Two authoritative systematic reviews in the Cochrane Library provide a definitive summary of the contemporary state of the evidence.

For migraine (Linde et al., 2009a), the authors identified 22 trials meeting the inclusion criteria. Six trials compared acupuncture to routine care (this included the cohort of patients with migraine from the ARC trial described earlier), and meta-analysis showed clear evidence of benefit from acupuncture at 3–4 months. Fourteen trials compared acupuncture with a variety of sham interventions, with no clear evidence of superiority of acupuncture over sham. Four trials compared acupuncture with prophylactic drug treatment, with results for 'response', number of migraine attacks, number of migraine days and headache intensity significantly in favour of the acupuncture groups at various time windows. In all four trials, more patients receiving drug treatment reported adverse effects than patients receiving acupuncture, but the difference was less pronounced in the largest trial and heterogeneity was significant.

Overall, this review concludes that acupuncture should be considered as a treatment option for migraine patients, particularly those who experience adverse effects from drug treatment. However, the fact that true acupuncture is not superior to 'sham' suggests (as has already been noted) either that accurate needle placement may not be as important as acupuncturists have traditionally thought, or that the benefits of acupuncture may be largely ascribed to 'placebo' factors.

## Clinical points

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High quality evidence shows acupuncture clearly effective for tension headache and migraine, though the effect is not point specific in migraine. Guidelines recommend acupuncture for headache.

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For tension-type headache (Linde et al., 2009b) the evidence base is smaller but the results of the systematic review are if anything even more positive. Eleven trials met the inclusion criteria. Two trials compared acupuncture to routine care. These were the ART trial and the cohort of patients with tension-type headache in the ARC trial, both described earlier: both found significant benefit of acupuncture in terms of 'response', number of headache days and pain intensity at 3 months. Six trials compared acupuncture with a sham intervention, and meta-analysis showed small but statistically significant benefits of acupuncture over sham on most outcome measures (response, headache days, headache intensity and analgesic use) at various time windows. Four trials compared acupuncture with other physical treatments (primarily physiotherapy or relaxation); due to methodological issues the results were difficult to interpret, though one rigorous trial suggested if anything better short-term outcomes for relaxation than acupuncture but no long-term differences between treatments (Söderberg et al., 2006).

Overall, this review also concludes that acupuncture could be a valuable non-pharmacological tool in patients with frequent episodic or chronic tension-type headache.

Furthermore, a large meta-analysis of acupuncture for chronic pain was performed by Vickers et al. (2012). Only rigorous trials in which allocation concealment was unequivocally robust were included, and the individual patient data were subject to meta-analysis. In the chronic headache arm of this investigation, the German trials plus the author's own trial (Vickers et al., 2004) were included and acupuncture was found to be statistically superior to either sham or no acupuncture.

## MECHANISM OF ACTION

As mentioned earlier, the pathogenesis of both common types of headache is poorly understood, but headache can be regarded as a chronic pain condition, and the spinal trigeminal nucleus (the dorsal horn for the head) is known to be more sensitive (more subject to 'wind-up') in patients with chronic headaches. For a detailed neurophysiological discussion of the mechanism of action of acupuncture in chronic pain the reader is referred to Chapter 3.

## SUMMARY

There is strong evidence that acupuncture is an effective intervention for both migraine and tension-type headache, though acupuncture may not be superior to 'sham' acupuncture for migraine. NICE, the English National Institute for Health and Clinical Excellence (2012) has endorsed the use of acupuncture in this context; its guideline on headaches recommends a course of up to 10 acupuncture treatments over 5–8 weeks for the prevention of chronic tension-type headache and chronic migraine.

## Epilepsy

### INTRODUCTION

Epilepsy is a common neurological disorder for which drug treatment is frequently unsuccessful, only about 70% of sufferers becoming completely seizure free. In China, acupuncture is widely used as a treatment modality, and some historical observational studies support its use. For example, Shi et al. (1987) treated 98 patients with poorly controlled epilepsy using scalp acupuncture and showed a significant reduction in seizure frequency in 66%.

### MECHANISM OF ACTION

Evidence from animal studies supports a possible mechanism. The neuropeptide cholecystokinin octapeptide (CCK8) is known to have anti-epileptic activity, as well as anti-opioid activity

(Dadar et al., 1984). In experimental rats, Oei et al. (1992) showed that pretreatment with a CCK8 antagonist greatly enhanced the analgesic effect of high frequency (100 HZ) EA, though not low-frequency EA, suggesting that the analgesic effect of high frequency EA is antagonised by CCK8 release during stimulation. Further, a strain of rats bred to be susceptible to acoustically-evoked epileptic seizures had an unusually strong analgesic response to EA which was not potentiated by CCK8 antagonism, suggesting that a functional deficit of CCK8 might be relevant to susceptibility to epilepsy. This points to a possible theoretical mechanism by which high frequency EA might enhance CCK8 release and exert an anti-epileptic effect in humans.

## EVIDENCE

Unfortunately there is very little experimental evidence to support the use of any form of acupuncture for this indication. The only noteworthy trial in the Western literature is that of Kloster et al. (1999). Twenty-nine patients were randomised to classical acupuncture at LR3, LI4 and GV20 plus additional points chosen according to TCM diagnosis, or sham acupuncture at three points considered non-active. Both groups showed a small but non-significant reduction in seizures per week and also a small increase in seizure-free weeks that was significant only in the sham group. Cheuk and Wong (2014) conducted a review for the Cochrane library of acupuncture for epilepsy, including all randomised trials in which acupuncture was compared with sham treatment, anti-epileptic drugs or no treatments, or in which acupuncture was compared as an additional treatment to any other modality. Apart from the trial already mentioned, 16 Chinese trials were included, some of which used catgut implantation at acupuncture points rather than conventional acupuncture; none used high frequency EA. All trials had a high risk of bias and short follow-up.

## SUMMARY

This Cochrane review concluded that current evidence does not support the use of acupuncture as a treatment for epilepsy. Acupuncturists should also bear in mind the very small risk of acupuncture provoking an epileptiform seizure – this occurred once in 31 822 treatments in the major survey of White et al. (2001) (see Chapter 14: Safety).

## Spinal cord injury

There is some evidence to support the use of acupuncture in spinal cord injury, both from basic science and clinical trials.

## EVIDENCE

In a clinical trial from Taiwan of 100 patients with severe acute spinal cord injury and complete motor paralysis (American Spinal Injury Association grade A or B), patients were randomised to receive acupuncture in addition to standard rehabilitation or standard rehabilitation alone (Wong et al., 2003). The acupuncture intervention consisted of EA at 75 Hz applied to adhesive surface electrodes at points SI3 and BL62 bilaterally; this unusual technique was chosen because of theoretical concerns that needling might cause autonomic hyperreflexia in these patients. This was combined with auricular acupuncture at four ear points related to the spinal cord, using indwelling studs changed weekly. Treatment sessions lasting for 30 min five times weekly were started immediately, either in the emergency room or soon after surgery and were continued until discharge. Highly significant differences were seen between the acupuncture and control groups on measures of motor and sensory function as well as functional status, both at discharge from hospital and at follow-up 1 year postinjury. There is limited evidence also for a beneficial effect of acupuncture

on bladder and bowel function as well as chronic pain following spinal cord injury (Dorsher and McIntosh, 2011).

A recent meta-analysis reviewed all published randomised controlled trials of acupuncture for spinal cord injury and its complications (Heo et al., 2013). Sixteen trials were included, of which 12 were Chinese, two Taiwanese including the one discussed earlier and two American. Eight trials studied functional recovery: six looked at bladder dysfunction, and two examined the use of acupuncture for shoulder pain. There were methodological issues with most studies, and only two were of high quality. With this caveat, there were positive results for the use of acupuncture combined with conventional treatments for functional recovery when compared to conventional treatments alone. There were also positive results for the treatment of bladder dysfunction, as measured by total efficacy rate, for acupuncture compared to conventional treatments. The two trials of acupuncture for shoulder pain after stroke did not show a benefit over sham acupuncture or a conventional treatment programme. These results are encouraging, but clearly higher-quality studies are required.

## MECHANISM OF ACTION

In an animal model of spinal cord injury, rats with a T8 spinal cord contusion treated with EA at BL60, BL54 and GV3 within 15 min of surgery (but not 24 h postsurgery) showed less shrinkage of the cord and relative preservation of anterior horn cells below the lesion (Politis and Korchinski, 1990).

As in stroke research, recent work is beginning to reveal the mechanism by which acupuncture might be neuroprotective in spinal cord injury. In a rat model of spinal cord injury, Jiang et al. (2014) studied EA at 2 Hz, manual acupuncture and transcutaneous acupuncture point electrical stimulation also at 2 Hz, all treatments being administered to points CV26 and CV16 for 30 min at 2 and 8 h postsurgery. All three treatments led to some preservation of tissue morphology on histological staining. Further, all three treatment groups demonstrated increased antioxidant function, reduced expression of pro-inflammatory cytokines and reduced apoptosis, with EA being significantly more effective than manual acupuncture or transcutaneous acupoint electrical stimulation (TEAS) on all these measures. In a similar study in rabbits, Renfu et al. (2014) showed that EA at 20/40 HZ for 15 min at points BL54, ST28, CV6 and CV3 daily for 3 days after spinal cord injury inhibited neuronal apoptosis and increased the expression of anti-apoptotic signalling pathways.

## SUMMARY

One noteworthy trial supports the use of acupuncture to promote functional recovery in acute spinal injury. It is perhaps surprising that more high quality work has not been published in this field, as it appears worthy of further study. As in stroke, animal studies are beginning to reveal the mechanisms by which acupuncture may be neuroprotective.

## Multiple sclerosis

There is as yet no significant body of empirical or experimental evidence to support the use of acupuncture in multiple sclerosis, though there are individual case reports showing benefit (Foell, 2011) and evidence that acupuncture may improve fatigue in some patients (Foroughipour et al., 2012).

## Neurodegenerative disorders

To the Western medical mind, it might initially seem implausible that acupuncture could have a role in Parkinson's disease and Alzheimer's disease, two of the major neurodegenerative diseases.

Indeed there is a paucity of clinical evidence for its use. However, animal studies may point towards a way forward.

One theory of the pathogenesis of Parkinson's disease is that cell damage in the substantia nigra is the result of oxidative stress, and evidence for this comes from the effects of the neurotoxin MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) which causes a Parkinsonian syndrome both in man and in experimental animals. In a mouse model of Parkinson's disease, Wang et al. (2011) showed that the toxic effects of MPTP on the substantia nigra are ameliorated by daily 100Hz EA applied bilaterally to ST36 and PC6, commencing prior to MPTP administration. Mice pretreated with EA in this manner showed reduced neuronal loss in the substantia nigra and increased striatal levels of dopamine and its metabolites, accompanied by reduced levels of free radicals and increased levels of antioxidants.

Similarly, in a mouse model of Alzheimer's disease, Li G et al. (2012) showed that manual acupuncture using CV17, CV12, CV6, SP10 and ST36 bilaterally, performed daily for 15 days, not only reduced neuronal loss in the hippocampus but also improved the animals' performance on a behavioural test.

These animal studies suggest that acupuncture might potentially alter the pathological process in Parkinson's and Alzheimer's disease. This is all the more remarkable when one considers that while drug treatments for Parkinson's disease are highly effective at ameliorating the symptoms (those for Alzheimer's disease less so), no pharmacological intervention for either condition has as yet been shown to alter the disease process or outcome. While these animal experiments may appear far removed from routine clinical practice, they may provide a tantalising glimpse of therapeutic possibilities to come.

## Concluding comments

The role of acupuncture in reducing the symptoms of self-limiting neurological conditions such as tension-type headache and migraine is established as clinically useful. Although the evidence for a major role of acupuncture in stroke rehabilitation is not supported by evidence, laboratory studies suggest that acupuncture, particularly EA, may have a neuroprotective activity and well-designed clinical studies in conditions such as spinal cord injury are eagerly awaited.

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# Acupuncture in mental health

P.B. Ronan ■ H. Rampes

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## Introduction

Mental health service users are keen for complementary and alternative therapies such as acupuncture to be made available to them. People suffering from mental illness are high users of complementary and alternative therapies (Hunt et al., 2010; The Mental Health Foundation, 2011; Werneke, 2009). We are beginning to understand how acupuncture works in the management of pain and cell repair. There has been progress in the investigation of acupuncture as a treatment for mental illness. This chapter outlines the evidence for the use of acupuncture in the treatment of mental illness.

The mechanisms of acupuncture's effects in mental illness can be seen in relation to other therapies. Psychotropic medication is an important treatment modality in mental illness, modulating brain neurotransmitters, principally the monoamines (Gelder et al., 2006) and leading to neuroplastic effects. For example lithium carbonate which is commonly used in the treatment of bipolar disorder has been shown to promote neurogenesis (Chen et al., 2000).

Acupuncture modulates neurotransmitters in the brain, including endogenous opioids and serotonin (Bosch and Van den Noort, 2005; Bosch and van den Noort, 2008; Dhond et al., 2007; Yoshimoto et al., 2006). Functional magnetic resonance imaging studies have shown that acupuncture affects the limbic-paralimbic-neocortical network, which plays a key role in regulation of emotion, cognition and processing memories (Fang et al., 2009). Stroke research suggests that acupuncture has the potential to stimulate cell regeneration in the brain (Bosch and Van den Noort, 2005; Dhond et al., 2007). In addition, raised cortisol levels are associated with stress, anxiety, depression and schizophrenia and other psychiatric disorders (Gelder et al., 2006; Gunduz-Bruce et al., 2007; Reid and Watson, 2006; Ritsner et al., 2007; Walder et al., 2002). They may

be lowered by acupuncture (Akimoto et al., 2003; Harbach et al., 2007; Huang et al., 2011; Schneider et al., 2007). If acupuncture has such effects on the brain, then it is plausible that it may influence mental illness and could be used as part of the portfolio of treatments available.

## Depression

Depression presents a serious, worldwide challenge for health services (World Health Organization, 2012). Between 5% and 10% of the population suffer from depression at any one time (Ohayon, 2007; Stordal et al., 2003), and 0.7–2.9% have major depressive disorder (Stordal et al., 2003; Wang et al., 2010). In Europe, lifetime risk of suicide attempt for people with major depressive disorders is reckoned to be around 28% (Bernal et al., 2007). Depression causes a significant burden of disease with a proportion of patients responding poorly to current treatments (World Health Organization, 2007). It is associated with heart disease (Gowrishankar, 2011; Nemeroff et al., 1998), addictions (Hasin, 2005), stroke (Zavoreo et al., 2009) and dementia (Enache et al., 2011; Lenoir et al., 2011). It is more prevalent in women than men, although this is not necessarily associated with changes in sex hormones over the life-span (Ronald, 2003). People who present with pain are four times more likely to have depression or anxiety as well (Lépine and Briley, 2004).

Although psychosocial interventions are increasingly available and effective for people with depression (Lau, 2008), for many there is an underlying biological cause that needs a biomedical solution. Treatment with antidepressant medication is not always effective or safe. Selective serotonin re-uptake inhibitors (SSRIs) such as fluoxetine, paroxetine and citalopram, which are most commonly used to treat depression, are known to cause nausea and erectile dysfunction, as well as insomnia and agitation in the elderly. Initial weight loss, followed by weight gain in the long term is associated with SSRIs (Westenberg and Sandner, 2006). Studies have revealed that antidepressant medication exposure in pregnancy has been associated with congenital malformations, spontaneous abortion, preterm birth and abnormal birth and neonatal adaptation difficulties. There is concern about persistent pulmonary hypertension in the neonate (Udechuku et al., 2010). However, a more recent study of 63 395 women from the Norwegian Mother and Child Cohort Study did not suggest that there was a strongly increased risk of malformations, preterm birth, or low birth weight following prenatal exposure to antidepressants (Nordeng et al., 2012). People suffering from chronic depression tend to have poor socio-economic backgrounds, and take longer to access specialist treatment than those with a normal course of major depressive disorder (Rubio et al., 2011). Light therapy is used in the treatment of seasonal affective disorder, a variant of depressive illness disorder (Lau, 2008). Electro-convulsive therapy (ECT) is usually reserved for people suffering from severe depression and can be life-saving in such cases where people have stopped eating and drinking. ECT unfortunately causes short term memory impairment in some cases (Mayor, 2003).

There have been a number of trials investigating acupuncture in the treatment of depression. However, these tend to be under-powered, heterogeneous and biased in terms of blinding (Schroer and Adamson, 2011; Smith et al., 2010; Wang et al., 2008). We examine some recent studies.

Andreescu and colleagues (2011) used a blind randomised parallel group design to compare the efficacy and tolerability of electro-acupuncture with a sham (control) acupuncture for mild to moderate depression in 57 patients. There was little difference between the two groups in terms of outcomes for depression. Both treatment approaches achieved a reduction of 7.4 and 7.9 respectively on the Hospital Anxiety and Depression Scale (HADS), which is a significant improvement (Andreescu et al., 2011). Vasquez and colleagues (2011) conducted a double blind randomised controlled trial (RCT) testing sham against real acupuncture for the treatment of major depressive episode in 42 patients. They carried out salivary cortisol measurement as well as clinical evaluations, primarily the Carroll Rating scale. They too found a significant reduction in depression coupled with a normalisation of saliva cortisol (Vázquez et al., 2011). Both of these

studies would have benefitted from a third, no acupuncture, arm in order to control for the effect of sham acupuncture. Although they used fixed treatment protocols (based on different rationales), there has been an argument for using individualised acupuncture in such studies in order to mimic the normal experience of treatment (Schroer and Adamson, 2011). It is not clear how the blinding was conducted in the latter study.

A research team in the US introduced two significant developments in trial methodology: individualised Traditional Chinese Medicine acupuncture was applied using a 'manual' to select treatment for particular symptoms that would be reproducible, and two acupuncturists were involved in treatment. The first prescribed a treatment for each patient, together with a second formula that was considered ineffective for depression but plausible in itself. One of these was chosen at random and applied by the second acupuncturist; thus achieving double-blinding (participant and therapist). In one study, by Allen and colleagues (2006), 151 participants with major depressive disorder were recruited to a three-arm double blind randomised controlled trial – the third arm was a waiting list control. Following 8 weeks of treatment, the response rate to acupuncture was 22%, and to sham it was 39%. Both reached 50% after 16 weeks of treatment. Whilst both of these were better than the waitlist control, neither represented an encouraging result that would support acupuncture as a sole therapy. Moreover, the success of sham over the real acupuncture only serves to confound questions about the efficacy of acupuncture for this condition (Allen et al., 2006).

### Clinical points

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Trials of acupuncture for depression have used separate practitioners for diagnosis and treatment to achieve double-blinding.

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Using similar methodology, Manber and colleagues reported two three-arm studies in 2004 and 2010, in 61 and 150 pregnant women respectively. In the latter study, the raters were also blinded. The arms received genuine acupuncture, acupuncture not specific to depression and massage. All three arms resulted in improvements in depression, with the genuine treatment arm showing significantly greater improvements than either non-specific acupuncture or massage. Participants were followed up 10 weeks postpartum and had retained these improvements. The size of effects seen in the specific arm is equal to or better than those of antidepressants and psychosocial therapies (Manber et al., 2004, 2010).

In a large, three-arm pragmatic RCT in primary care (MacPherson et al., 2013), 755 patients with depression were randomised to acupuncture, counselling and usual care alone. Patients attended a mean of ten sessions for acupuncture and nine sessions for counselling. Compared to usual care, there was a statistically significant reduction in mean Patient Health Questionnaire (PHQ-9) depression scores at 3 and 12 months both for acupuncture and counselling which were both significantly better than usual care alone, but not different from each other.

Evidence that acupuncture might be more effective than, or enhance the effects of, antidepressants is available from several studies. Notably, Fu and colleagues (2008) conducted a randomised controlled trial of 440 patients with major depressive disorder from four hospitals. Here they compared acupuncture of two specific points, Hegu (LI 4) and Taichong (LR 3) aimed at depression with non-specific acupuncture and a therapeutic dose of fluoxetine. Measurements included the Hamilton Rating Scale for Depression, the Asberg's Anti-Depressant Side-Effect Rating Scale and severe adverse reactions to acupuncture. The overall outcome for depression orientated acupuncture was more effective than either arm in the study (86%: 59%: 73% respectively) and included no severe adverse reactions to acupuncture. Changes in the Hamilton Rating Scale for Depression were similar to fluoxetine (Fu et al., 2008), but adverse events were significantly lower with acupuncture. Similar findings were noted on a study of 75 participants by Duan et al. who included an arm to test electro-acupuncture and fluoxetine combined. The participants in this group fared better, including

having fewer side-effects from the antidepressant, than those in either the electro-acupuncture or antidepressant alone groups (Duan et al., 2008). A German study corroborates these latter findings when testing acupuncture with a tricyclic antidepressant (Röschke et al., 2000). However, all of these studies have questions around their allocation concealment and blinding.

There remains some questions about whether acupuncture will be acceptable to the wider population of depressed patients, since studies have been conducted in various specific subgroups, either of just one sex, or at extremes of depression, and commonly in in-patients (Schroer and Adamson, 2011). Moreover, only two studies to date (Manber et al., 2004, 2010) have included long-term follow up, and none of the studies have included data on changes in quality of life (QoL). Future studies might go further than giving attention to bias and blinding, for instance by including measurements of QoL, and specifically exploring the effect of acupuncture on female hormones in relation to low mood.

The Cochrane review of depression (Smith et al., 2010) is a rigorous systematic review which concluded that ‘there was a high risk of bias in the majority of trials. There was insufficient evidence of a consistent beneficial effect from acupuncture compared with a wait list control or sham acupuncture control’. However, the authors point out that ‘two trials found acupuncture may have an additive benefit when combined with medication compared with medication alone’. In a thoughtful commentary on the Cochrane review, Schnyer (2011) concluded that ‘data is still insufficient not only to confirm but also to refute the potential clinical application of acupuncture for depression’.

## BIPOLAR DISORDER

Studies on acupuncture in the treatment of bipolar affective disorder are rare. Of interest is the study conducted by Dennehy and colleagues between 2000 and 2003 (Dennehy et al., 2009). Through advertisements in local newspapers and health food shops, they recruited 20 participants who were in a manic phase and 26 in a depressive phase. Both cohorts were split into two groups, one of which was treated with acupuncture targeted at their condition, and one with an acupuncture control. All of the participants were treated with psychotropic medication (mainly sodium valproate for mood stabilisation), which remained constant for the study period. Fifty percent of those who were manic and 27% of those who were depressed were withdrawn, mainly because of worsening in their condition and, for the manic participants, difficulty in adhering to the study protocol. The remainder all experienced improvements in their baseline symptoms. The report does not detail the medication dosages or length of time that was taken prior to participants beginning treatment. Overall, the team experienced unforeseen difficulties in recruitment (lack of enthusiastic response from service users), retention (from the erratic behaviour of people who are manic and the anxious responses of clinicians when patients are deteriorating), and implementation of the study protocol (confusion in application of acupuncture by week 5 of the study). On careful reading, it seems that the psychotropic medication had begun to work, rather than the acupuncture.

## CLINICAL APPROACH

From a Western perspective, the appropriate dose and schedule of acupuncture is probably of importance for treating depression, and most protocols describe eliciting *de qi* and leaving needles for 20 min. Typical points used include GV20, PC6, HT7, ST36, SP6, SP4 and LR3. Electro-acupuncture is frequently used in studies conducted in China.

## Anxiety

Anxiety is a normal reaction that can become problematic in certain situations, such as going to the dentist, having a medical procedure or competing at a sports event. Anxiety disorders range from acute stress reaction, adjustment disorders, generalised anxiety disorder, panic disorder, social phobia, post-traumatic stress disorders and autism. Anxiety symptoms do occur and can be

severe in depressive disorders, bipolar disorder and schizophrenia. Generalised anxiety disorder is thought to affect around 4.4% of the population in the UK (McManus et al., 2009) and between 0.8% and 6.4% of the population worldwide (Grant et al., 2004; Kessler et al., 2006; Lieb et al., 2005). People with anxiety are more likely to visit their doctor and consult medical specialists, particularly in gastroenterology (Kennedy and Schwab, 1997; Wittchen et al., 2002). Treatment involves psychological treatments (e.g. cognitive behaviour therapy) and antidepressant medication. However, neither is completely satisfactory, and there is a consistent group of people for whom none of these therapies works (Errington-Evans, 2009; National Collaborating Centre for Mental Health, 2011).

The evidence for acupuncture in the treatment of anxiety looks promising in dentistry, surgery and sports medicine, as well as several rat model experiments. However, there is a dearth of studies (Pilkington et al., 2007) and although a number of recent studies have been carried out either specifically on anxiety (e.g. Acar et al., 2013; Bussell, 2013; McPherson and McGraw, 2013) or including anxiety measurements (e.g. Reshef et al., 2013; Smith et al., 2014; Wang et al., 2013), methodological problems continue (Bussell, 2014). Studies have been criticised for their poor methodological quality and heterogeneous nature, but the statistically significant positive outcomes contained in most of these studies cannot be ignored (Bussell, 2014; Pilkington, 2010; Pilkington et al., 2007).

### Clinical points

Moderate evidence suggests acupuncture is effective for treatment of situational anxiety in dentistry, surgery and sports medicine.

Wang and colleagues conducted a randomised controlled trial on 56 patients undergoing lithotripsy. Participants received either real point or sham point auricular acupuncture with press needles before the procedure followed by either real (2–25 Hz) or sham electro-acupuncture at LI4 and LR3 during the procedure – using superficial insertion in the sham group. The rater and the participants were blinded to the intervention. Participants were asked to complete a State and Trait Anxiety Inventory on admission and 30 min after having auricular acupuncture (preoperatively). During the procedure, participants could ask for extra analgesia. After the procedure they completed a visual analogue scale to pain, and prior to discharge, were asked whether they believed they had received real or sham acupuncture. The results showed that those receiving real acupuncture had significantly less anxiety ( $p=0.029$ ), felt less pain ( $p=0.221$ ) and needed less analgesia ( $p=0.040$ ) than those in the sham group (Wang et al., 2007). This was a small study which might have benefited from a third arm where participants were given no acupuncture. There have been similar findings in a preoperative cataract study in 25 patients, using three arms (real, sham and no acupuncture). Real acupuncture was found to reduce anxiety significantly more than both the sham and no acupuncture groups. Sham treatment showed some effect post-treatment, but real acupuncture retained its significance over no acupuncture (Gioia et al., 2006).

Several studies have shown that acupuncture reduces cortisol levels in stressful situations. Akimoto and colleagues proposed that acupuncture would inhibit a decrease in physical well-being induced by physical exercise. They studied 21 elite soccer players during a 3-day tournament, nine of whom were given acupuncture, the remaining 12 players were the control group. The treatment group was given 2 h of acupuncture 1 day before the tournament and again each evening of the tournament, before the game. Saliva samples were collected from all players 1 week before the tournament, on all 3 days of the tournament and again 3 days after the tournament. Subjects were also asked to complete questionnaires on their physical and emotional well-being. They were given a profile of mood states questionnaire to ascertain their emotional well-being. This measures tension, depression, anger, vigour, fatigue and confusion. The result was that the cortisol concentration significantly increased in the control group in days 2 and 3,

whereas in the treatment group, it increased on day 1 but decreased to baseline in days 2 and 3. Overall, cortisol was significantly lower for the treatment group than for the control group. The subjects' experience of physical and mental well-being reflected this finding. The treatment group reported significantly less muscle tension and suffered from less fatigue and confusion than the control group (Akimoto et al., 2003).

In another study, Schneider et al. explored the specific effect that acupuncture has on the neuroendocrine and autonomic nervous system. Using a randomised sham-controlled trial, they administered either real or sham acupuncture to 34 patients who were being treated for irritable bowel syndrome. Saliva was collected for examination before treatment began and at regular time points during treatment. Patients were also asked to complete two QoL questionnaires before, immediately after and 3 months after treatment. They found that salivary cortisol decreased in both groups, with the drop in the real acupuncture group being higher but not statistically significant. QoL improved in both groups, but the differences were not significant (Schneider et al., 2007).

Sweating can be a symptom of stress and can be induced in controlled trials where subjects are placed in situations that are stressful. Here subjects can be exposed to loud noise, pain, mental arithmetic or memory testing in order to induce 'mental induced sweating'. Several studies show that acupuncture can reduce sweating from the palms of the hands and the soles of the feet (Hsieh, 1998; Ogata et al., 2002, 2005, 2007). In one experimental study, Ogata and colleagues examined the effect of electro-acupuncture on sweating when given at different frequencies. A total of 25 healthy volunteers, divided into two groups, took part in two experiments. Baseline sweat levels were taken and the subjects underwent two-minute mental arithmetic tests whilst having electro-acupuncture at various intervals over half an hour. Electro-acupuncture was administered at two frequencies 5 and 100 Hz. They found that both frequencies reduced sweating during treatment, but this was not sustained for long after treatment. They also found that treatment at the higher frequency was ineffective in one of the experiments and only partially effective in the other (Ogata et al., 2005). These results are similar to those found in other studies. However, these were uncontrolled studies and used sweating as a proxy for anxiety itself, which is a limitation.

## CLINICAL APPROACH

The points *Yintang* and GV20 (with or without *Shishencong*) are common to many treatments described for anxiety, and *Yintang* alone may have immediate benefit in acute anxiety. Auricular points such as *Shenmen* are often added. Auricular *Shenmen* or *Yintang* may be used alone for situational anxiety, for example for dental procedure. Other points are used, for example HT7, PC6, BL62, ST36, ST25, LI11 and dorsal points including GV4 and BL23. Traditionally, a series of Bladder meridian points were used, such as BL13, BL15, BL17, BL18, BL20 and BL23 or a combination of GB13 and GV24. The schedule may need to include frequent treatments, some authors recommending several times a week.

## Dementia

Dementia is thought to affect over 24 million people worldwide, and its prevalence is set to almost double by 2020 (Brayne et al., 2011; Ferri et al., 2005). Alzheimer's disease is thought to be the most prevalent cause, followed by vascular dementia (2014). Other types include dementia with Lewy bodies, frontotemporal dementia, vascular dementia, dementia associated with Parkinson's disease, and mixed dementias. Symptoms include memory loss, language impairment, disorientation, changes in personality, difficulties with activities of daily living and self-neglect. Dementia sufferers may also suffer from a co-morbid mental illness such as depression, anxiety or psychosis (Nice, 2006, amended March 2011). There is some evidence to support the role of psychosocial interventions and medications (both herbal and conventional) in stemming the progress of the disease, but there is no known cure (Brayne et al., 2011; Brodaty et al., 2011).

A Cochrane review of acupuncture for vascular dementia (Peng et al., 2007) found 95 studies, 94 of which were Chinese. There were 17 RCTs, of which 16 were excluded (one is still being assessed). Reasons for exclusion were use of either an unproven Western medicine or another therapy alongside acupuncture and inadequate randomisation. Lee and colleagues found 40 RCTs also originating in China, three of which met their inclusion criteria. However, they criticised these multiple armed trials for poor methodological quality because of poor reporting of the methods. The review fails to mention any efforts by the team to contact the relevant researchers in order to check methodology. Nevertheless, they report on some of the findings of the studies, which include both positive outcomes and no significant effect of acupuncture over the various controls used in the studies (Lee et al., 2009a).

In a review that is more informative for practitioners, Cheng and Cheng outline the research that has been carried out over the past 10 years (Cheng and Cheng, 2009), focussing on the clinical approaches, rather than the research methods. The studies, small and non-randomised, all show high rates of success for acupuncture alone or combined with another treatment. There is promising evidence for the use of acupuncture for many of the symptoms of dementia. Researchers will have to address issues of randomisation, blinding and types of outcome measures relevant to the condition, as well perhaps as cross-cultural transfer of utility of acupuncture if we are to be certain of effect.

## Schizophrenia

Schizophrenia is a severe and debilitating condition that affects around 1% of the global population (McGrath et al., 2008). Its prevalence is set to increase, as it is associated with urbanisation and poverty (Pedersen and Mortensen, 2001; Peen and Dekker, 1997; Sundquist et al., 2004). The condition leads to social isolation and poor physical health (Lambert et al., 2003), self-harm and suicide (Pompili et al., 2007). The onset of schizophrenia is usually in early adult life, with most patients being chronically ill for the remainder of their lives. The mainstay of treatment is with antipsychotic medication, with some emerging research showing that treatment with psychological therapies may be useful in the early stages (Freeman, 2011; Lewis et al., 2006). There have been improvements in antipsychotic medication in the last 15 years, but side-effects remain problematic. The main problems are that patients report experiencing side-effects that are so severe that they are, to them, worse than tolerating the original condition. The result of this is that long-term effectiveness of antipsychotic medication is reduced from 70% to around 36% because of non-compliance (Ross and Read, 2004). The older antipsychotics are thought to be effective in around 36% of cases (Ross and Read, 2004), and it has been reported that they are not significantly worse than the newer atypical antipsychotics in terms of treatment outcomes and QoL (Lewis et al., 2006).

In Europe, there has been some progress in building a study design for acupuncture and schizophrenia. A service user evaluation carried out in 2008 has had very positive results for this mode of treatment (Rogers, 2009). In European trials of acupuncture for schizophrenia, participants are often fully engaged. It may be the novelty of a treatment not normally available through the health service, or the availability of a treatment that is not ostensibly linked with psychiatry that generates this enhanced engagement, which is not normally seen in trials of other types of mental health treatments such as antipsychotics and talking therapies.

A prospective preclinical pilot study found positive outcomes for symptoms of schizophrenia and improvements in energy, sleep, weight, addictions and side-effects of antipsychotic medication (Ronan, 2011). This study highlights the dangers of treatments that cause rapid improvements in this vulnerable group. Two of the participants felt so well that they returned to previous addictive habits, one of them stopping his medication as well. Both suffered from acute relapses and took some time to recover. Small-scale studies have also been carried out in Germany and Israel, both confirming results of those in the UK (Bloch et al., 2010; Bosch et al., 2010).

Cheng et al. (2009) conducted a rater and participant blinded, two arm, randomised controlled trial on 60 acupuncture naïve patients with a DSM-IV diagnosis of schizophrenia. Participants were given either real or sham electro-acupuncture over 6 weeks alongside established, but ineffective antipsychotic treatment. Symptoms of psychosis were the primary outcome for measurement, followed by assessment of positive and negative symptoms of schizophrenia. Qualitative data was also collected, including medication use, sleep, anxiety and depression. Thirteen of the 30 participants in the real electro-acupuncture group experienced a  $\geq 20\%$  improvement in symptoms of psychosis. A significant reduction was achieved in positive and negative symptoms score by week 6. The sham group results were comparably less favourable (Cheng et al., 2009). The numbers in the study were not high enough to confirm statistical significance in either measurement, but this study is easily replicable and might well be used as a model for future work.

Several new studies have been completed in the last 10 years, mainly in China. Four reviews of studies have taken place since 1997 (Beecroft and Rampes, 1997; Harbinson and Ronan, 2006; Lee et al., 2009b; Rathbone and Xia, 2005), and each has concluded that acupuncture may help symptoms of schizophrenia, but evidence is hampered by poor reporting of and methodology in studies. Although the methodology has improved, numbers are still too low to know whether the effect that is seen in most studies can be generalised (Lee et al., 2009b). Moreover, as is the case for dementia studies, this area would benefit from further international studies to confirm Chinese findings (Lee et al., 2009b). In the most recent review, Lee and colleagues found 13 RCTs that met their criteria for review. All of the studies reported positive outcomes for acupuncture alone or alongside antipsychotic drugs. The review highlights issues of blinding, lack of reporting of ethical processes, culture-specific assessment of schizophrenia, and lack of investigation of the interactions between antipsychotic medication, dosage and side-effects with acupuncture.

## POSSIBLE MECHANISMS OF ACUPUNCTURE IN SCHIZOPHRENIA

Several explanations have been proposed for why or how acupuncture might help someone with symptoms of schizophrenia, but all are based on small, experimental studies. Extensive reviews carried out by Dhond and Bosch (Bosch and Van den Noort, 2005; Dhond et al., 2007) suggest the following.

Firstly, fMRI studies have shown that acupuncture can: modulate the limbic-paralimbic-neurocortical network, central to the regulation of emotion, cognition and memory processing (Fang et al., 2009; Hui et al., 2011); cause the release of endogenous opioids and serotonin (Bosch and Van den Noort, 2005; Bosch and van den Noort, 2008; Dhond et al., 2007; Yoshimoto et al., 2006); and can potentially cause cell regeneration in the brain (Bosch and van den Noort, 2008; Dhond et al., 2007).

Modulation of the limbic system might be key to ameliorating symptoms associated with schizophrenia. For example, co-ordination of responses in the amygdala, hippocampus and hypothalamus might improve negative symptoms of schizophrenia such as flattening of affect, arousal and motivation. In schizophrenia there is a strong possibility that glutamate may have a more important role than dopamine (Laruelle et al., 2003). N-methyl-D-aspartate (NMDA), which is the main receptor responsible for the binding and activation of glutamate in the postsynaptic cell, may become under-active in schizophrenia. Modulators of NMDA have been found to have an antipsychotic effect, whilst its antagonists have been shown to induce psychosis (Goff and Coyle, 2001). Some experimental pain studies show that the hippocampus and amygdala (where NMDA is present) are de-activated by acupuncture, whilst at least one study shows that it is possible to co-ordinate activation of these areas with other areas in the limbic system. This may be helpful for psychosomatic type conditions.

Secondly, studies on pain have clearly shown that acupuncture modulates and causes the release of endogenous opioids in the amygdala, hypothalamus and brain stem areas

of the brain. This may shift the balance of the autonomic nervous system, thereby reducing stress. Modulation of the hypothalamus in particular might result in decreased levels of cortisol and increase of dehydroepiandrosterone (DHEA), both associated with stress reduction. Low levels of DHEA are associated with stress and anxiety (di Michele et al., 2005; Reid and Watson, 2006).

There is some evidence that people with schizophrenia who self-medicate with opiates and opioids gain improvement in negative and positive symptoms of schizophrenia (American Psychiatric Association, 2004; Davis et al., 1977; Heinze et al., 1997; Mititelu, 2009; Schmauss and Emrich, 1985). It is thought that opiates have greater effect on positive symptoms, acting on the negative ones as well, whilst opioids mainly improve negative symptoms. The reason for this remains unclear. The most promising explanation for the role of opioid regulation in schizophrenia may lie with kappa opioids. Kappa opioids inhibit glutamatergic transmission in the nucleus accumbens shell. In schizophrenia there is thought to be disinhibition of glutamatergic projections to hippocampal and cortical areas resulting in progressive excitotoxic neuronal cell death (Deutsch et al., 2001). Regulation of this would stop or prevent the progressive degeneration of neurons, improve negative symptoms and cognitive deficits.

Thirdly, studies on patients with chronic stroke have shown that acupuncture produces hyperactivation in the area of the sensorimotor cortex related to the weakened side. This increase in activity was positively correlated with improvements in movement of the affected hand and upper limb. This shows that there is the potential for cell regeneration in the brain, including the potential for acupuncture to strengthen activity in the left side of the brain (Bosch and Van den Noort, 2005; Bosch and van den Noort, 2008; Dhond et al., 2007).

## CLINICAL APPROACH

The treatments used for anxiety and depression are also applied to schizophrenia.

### Side-effects of psychotropic medication

Side-effects of psychotropic medication are problematic (Ross and Read, 2004), a principal reason why 50% of patients do not comply with treatment, resulting in high rates of relapse (Ohlsen et al., 2003). Antipsychotic medication is probably the most problematic group, followed closely by mood stabilisers such as lithium carbonate and antidepressants. Amongst the undesirable side-effects of these medicines are drowsiness, dry mouth (or, in the case of clozapine, hypersalivation), excess thirst, increased appetite, weight gain, dizziness, constipation, hypertension and hypotension. Older antipsychotics are more likely to cause Parkinsonian symptoms, tardive dyskinesia, akathisia, constipation and weight gain. Side-effects of the newer antipsychotics are more detrimental to the long-term physical health of patients. These include weight gain, diabetes, dyslipidemia, ischaemic heart disease (Mosby Inc., 2013; Stahl, 2008).

Two studies on acupuncture for side-effects are available. One compared fluoxetine alone with fluoxetine combined with electro-acupuncture and found significant improvements in side-effects of dry mouth, constipation, dizziness, headache, weakness in the limbs and diarrhoea (Liu et al., 2009). An exploratory study on the effects of acupuncture in schizophrenia patients taking antipsychotic medication (Ronan, 2011) found no significant changes in the Schizophrenia QoL Questionnaire. However, participants reported improvements in drowsiness and energy, reduced weight, increased exercise and decreased dizziness, nocturia, Parkinsonian movements, akathisia and tardive dyskinesia. These findings are reflected in other small scale studies on acupuncture in the treatment of people with schizophrenia: Reshef and colleagues found significant improvements in sleep, sleep efficiency, sleep latency and emotional state when they compared normal treatment with acupuncture twice weekly on 20 patients (Reshef et al., 2013).

These findings were born out in two small scale studies conducted in Germany, one on schizophrenia and the second on schizophrenia and depression (Bosch et al., 2010; Bosch et al., 2014). Perhaps the most striking account of improvements in the side-effects can be found in a study conducted by Atwood, who was using acupuncture to help 16 people with chronic schizophrenia to reduce smoking. Significant reductions in the side-effects of antipsychotic medication were observed, as well as a 50% reduction in cigarette smoking. These included earlier waking and time of getting up, improved motivation and engagement with domestic and other activities, reduced hostility, and reduced extra-pyramidal side-effects. One member of staff was quoted: 'They're doing so well it's scary!' The patients were followed up over 7 years and maintained these improvements (Atwood, 1999).

## EVIDENCE FROM STUDIES IN NON-PSYCHIATRIC PATIENTS

Acupuncture has been studied for xerostomia (see Chapter 34). In a systematic review Jedel concluded that, although some studies have positive results, numbers of participants and methodologies used were too weak to confirm efficacy (Jedel, 2005). Since then there have been a few small scale RCTs (Braga et al., 2011; Cho et al., 2008; Meidell and Rasmussen, 2009; Simcock et al., 2012). The most recent, Simcock, employed 145 cancer patients in a randomised cross-over trial comparing acupuncture for xerostomia with oral health education. Both subjective and objective measurements indicated acupuncture to be superior. In another study, fMRI identified bilateral activation of the salivary glands in real but not sham acupuncture (Deng et al., 2008). Drooling was found to be reduced in five children having tongue acupuncture in one study (Wong, 2002), but it was thought to be too difficult to replicate the acupuncture methods used (Meningaud et al., 2006). It seems promising to study acupuncture for xerostomia secondary to antipsychotic medication.

There are few studies available on the potential for acupuncture on weight control. The small studies that are available show positive results for weight loss as compared to no acupuncture (Richards and Marley, 1998; Shen et al., 2009) or sham acupuncture (Cabioglu et al., 2008). This latter study offers special interest for schizophrenia. Here the researchers found a concomitant reduction in lipoprotein A associated with cardiovascular disease in the real acupuncture group. There seems to be only one study on eating disorders available (Fogarty et al., 2010). In this uncontrolled pilot study, five anorexic and four bulimic participants experienced improvements in QoL, anxiety and perfectionism when given acupuncture alongside normal treatment.

There is some evidence that acupuncture lowers blood pressure (e.g. Li, 2002; Park et al., 2010; Pengfei and Xuemin, 2010; Zhang et al., 2009). Flachskampf et al. conducted a high quality, single blind, two arm randomised controlled trial on acupuncture and hypertension. One hundred and sixty participants were allocated to real or sham acupuncture. They found significant reductions in the blood pressure of the real as opposed to the sham acupuncture groups after treatment. At 3 and 6 months, blood pressure returned to baseline (Flachskampf et al., 2007). The overall evidence seems mixed (Chapter 23) and there seem to be no studies available of acupuncture for hypotension.

Two systematic reviews of acupuncture for Parkinson's disease concluded that acupuncture maybe helpful (Lam et al., 2008; Lee et al., 2008a). Recently Ren found significant improvements for acupuncture with co-beneldopa over co-beneldopa alone in the treatment of Parkinson's disease in 50 cases (Xiao-ming, 2008). Eng et al. reported improvements in QoL and depression, but worsening of motor function in an uncontrolled study of 25 patients (Eng et al., 2006).

Three reviews concluded that there is some evidence for acupuncture and insomnia but that there is a paucity of high quality trials in this field (Cao et al., 2009; Lee et al., 2008b; Yeung et al., 2009). Participants in the UK study on acupuncture and schizophrenia reported improvements in hypersomnia (Ronan, 2011). This is an area worthy of further investigation.

## Concluding comments

There is emerging evidence that acupuncture has a role in the treatment of mental illness as an adjunct and as a treatment modality in certain psychiatric disorders. Psychotropic medications are efficacious but often not effective since patients discontinue treatments usually due to side-effects. Acupuncture should be further researched to ameliorate some of these side-effects and thereby improve patients' QoL and adherence to treatment. The evidence base is increasing, but larger methodologically robust trials are needed. More experimental studies are required to elucidate mechanism of action.

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# Acupuncture for drug dependence and obesity

A. White

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## Introduction

Drug dependence is a lifelong, persistent condition that resists most forms of treatment. Abstinence depends on many factors, not all of them well understood, and relapse rates are high. This chapter discusses the possible roles of acupuncture as part of a multifaceted treatment approach to this highly complex condition. A final section addresses obesity which has some features of dependence such as the importance role of the 'reward centre', the nucleus accumbens (NA), in maintenance of the condition.

Research into acupuncture for drug dependence is particularly difficult because of high drop-out rates from trials, lack of good knowledge of acupuncture mechanisms in dependence, and (probably) the need for demanding treatment schedules.

The terminology used in the field of drug dependence tends to be both vague (e.g. addiction, chemical, substance) and emotionally loaded (e.g. misuse, addict). This chapter uses the terms as defined in an authoritative report ([BMA Board of Science, 2013](#)); the condition is best called the 'dependence syndrome', and the person is 'dependent on psychoactive drugs'.

The WHO disease classification ICD-10 sets six criteria for the dependence syndrome, any three of which are diagnostic:

- a strong desire or sense of compulsion to take the substance
- difficulties in controlling substance-taking behaviour
- a physiological withdrawal state when substance use has ceased or been reduced
- evidence of tolerance, such that increased doses of the psychoactive substance(s) are required in order to achieve effects originally produced by lower doses
- progressive neglect of alternative pleasures or interests because of psychoactive substance use; increased amount of time necessary to obtain or take the substance or to recover from its effects
- persisting with substance use despite clear evidence of overtly harmful consequences.

We refer here to drug use as it is less pejorative than the terms drug abuse, drug misuse, substance abuse or substance misuse. 'Illicit' drugs are substances of which the possession, production, sale or use is prohibited by national law based on international convention; use of other drugs is lawful. 'Harmful' use implies physical or mental damage and sometimes includes social consequences. 'Problem' drug use is defined in various ways, usually to mean use by injection or prolonged regular use of the drug, and sometimes to include HIV or hepatitis diagnosis. The word 'craving' is often used for strong desire or compulsion, but is not formally adopted in ICD-10.

Many psychoactive drugs exist, differing widely in their effects, their potential for dependence and their consequences. Hallucinogens, inhalants, sedatives, hypnotics and anxiolytics are mostly lawful and may result in psychological but not physical dependence. Similar to these are psychostimulants and cannabis, though these are mostly illicit in many countries. We are mainly concerned here with drugs of dependence, whether legal or illicit, falling into four groups: cocaine, alcohol, nicotine and opioids – 'opioid' is the preferred term as it includes synthesised forms, whereas 'opiates' are naturally derived.

The causes of dependence are multi-factorial. Detailed discussion is outside the scope of this chapter, but in summary there is known to be a substantial genetic component; co-morbidity often exists (so-called 'dual diagnosis') with psychiatric illness and personality disorder; and developmental, environmental and occupational factors all contribute to the condition.

The prevalence of illicit drug use is estimated at between 3.4% and 6.6% of the global adult population, of which about a tenth is problem use ([World Health Organization, 2010](#)). Cannabis and amphetamine-type stimulants are the most common. Of the legal drugs, about 1% of the world's population is dependent on alcohol, and about 30% of adults smoke ([World Health Organization, 2011](#)).

Drug dependence has major consequences for individual, family, society and country. It is associated with personal decline such as reduced attainment, poverty, violence, criminality and social exclusion, and neglect of family. Societal consequences include loss of productivity and income, traffic and workplace accidents; national consequences include political instability. The cost of illicit drug use, including enforcement, is about 2% of GDP in those countries which have measured it ([World Health Organization, 2010](#)). It is estimated that, in the UK, every pound spent on drug treatment services generates £3 savings in public costs, mostly accounted for by reduced crime ([BMA Board of Science, 2013](#)).

The health consequences of drug use, as well of the means of administration in some cases, are manifold, both psychological and physical. Worldwide, the serious adverse effects on health from alcohol and tobacco far exceed those from cocaine and opioids. Alcohol is the third leading risk factor for burden of disease in developed nations. Globally it causes an estimated 2.5 million deaths each year, including 9% of all deaths between the ages of 15 and 29 years ([World Health Organization, 2004](#)). Tobacco causes 6 million deaths annually, 12% of the total ([World Health Organization, 2011](#)). Illicit drugs cause about 200 000 deaths each year.

## Clinical points

Estimated annual deaths globally due to dependence on major drugs: alcohol – 2.5 million; tobacco – 6 million; illicit drugs – 200 000.

Treatment of this lifelong condition is best considered in two stages. Detoxification refers to the acute withdrawal period, when symptoms characteristic of the drug used are treated; we shall consider acupuncture's role. Alcohol withdrawal symptoms can be particularly severe and occasionally life threatening. Detoxification is often achieved with pharmacotherapy and typically lasts 3–5 days though much longer for some drugs such as methadone.

The second stage, rehabilitation, refers to the sustained period aimed at restoration of more normal neurological and behavioural function, known as *recovery*. During this time the person experiences intermittent craving and has increased susceptibility to relapse. Relapse is potentially dangerous since tolerance is diminished, so the habitual dose may be lethal. Relapse prevention receives significant attention in rehabilitation programmes. Substitution therapy is available for opioid dependence (e.g. methadone, naltrexone, buprenorphine) but not for cocaine. This chapter considers acupuncture's possible role. Successful rehabilitation involves therapeutic programmes which, for more severe dependence, are often residential. Counselling including cognitive therapy is widely used to address perceived underlying factors in dependence such as learned, negative behavioural patterns, deeply ingrained feelings of low self-worth, habits of self-medication for underlying psychiatric or physical medical problems and lack of family and community support.

The role of any health service is to support and treat the physical and mental needs of the whole population which includes drug users (BMA Board of Science, 2013). This chapter assumes acupuncture will only be used in conjunction with other health services, and considers the potential use of acupuncture needling mainly as a neurobiological intervention. The neurobiological needs are rather similar for all four drug groups, though the clinical settings will be different and in particular smoking cessation services are usually regarded as separate from services for other drugs of dependence.

Although the neurological effects of acupuncture on the reward system are given prominence here, acupuncture treatment and the setting in which it is offered can of course have wider beneficial effects that may be very relevant clinically in reducing dependence. Acupuncture can increase relaxation (Chang et al., 2010), allowing time for reflection, away from a using environment; it can act as a 'token' or symbol of various benefits including caring (e.g. therapeutic alliance) and the possibility of positive help (expectation); and acupuncture is seen by drug users as empowering (Brumbaugh, 1993).

## Acupuncture for dependence

The modern history of acupuncture for drug and alcohol dependence dates from 1970 when the Hong Kong anaesthetist Dr. Wen was preparing a heroin-dependent patient for craniotomy operation as treatment for drug dependence (Cui et al., 2008; Wen and Cheung, 1973). He administered electroacupuncture (EA) at four body points (in two pairs: LI4 and SI3; PC4 and TE9) and two auricular points (brain-stem and *Shenmen*) – all on the right side only. Within 30 min, the patient said that his withdrawal symptoms had disappeared, and he no longer wanted surgery. Wen went on to observe that patients in whom he used EA for pain relief during surgery reported reduced withdrawal symptoms during the recovery period (Wen and Cheung, 1973). He then conducted several trials, both uncontrolled and controlled, using just auricular EA, which provided some evidence of an effect on opiate withdrawal symptoms (Wen and Teo, 1975). These trials and other clinical reports suggested that acupuncture induced calmness, reduced withdrawal symptoms and decreased craving.

These observations coincided with the growing understanding of the endogenous opioids and of acupuncture's ability to stimulate their release, [Han and Terenius \(1982\)](#) tentatively suggesting that maybe acupuncture replaced the newly withdrawn exogenous opioids by stimulating release of their endogenous relatives. Acupuncture, particularly EA, reduced signs of withdrawal in animals rendered opioid dependent ([Han and Zhang, 1993](#)).

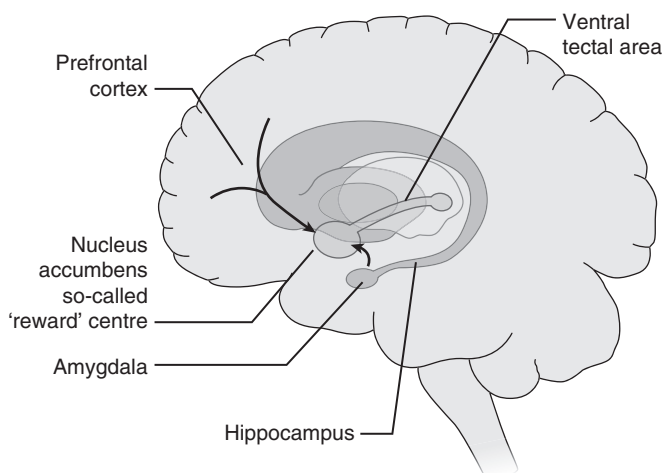
This convergence of basic research, laboratory studies and clinical evidence attracted publicity and stimulated the adoption of acupuncture for drug dependence. Acupuncture became even more practicable after the decision was made to discard EA based on the observation that manual stimulation alone was thought to be adequate ([Brumbaugh, 1995](#)).

Subsequent rigorous clinical trials, particularly those published in the watershed year 2002, found no difference between the effects on long-term abstinence of auricular acupuncture compared with stimulation of so-called 'inactive' auricular locations. However, despite these setbacks, acupuncture continues to be well regarded for its role in detoxification, being offered by 587 treatment facilities in the US (4% of the total) up from 400 in 2000 ([Office of Applied Studies SA and MHSA, 2009](#)).

Thus there appears to be a significant mismatch between positive clinical experience of acupuncture's benefits in withdrawal and the negative evidence from clinical trials testing underlying theory, which is addressed below in the section on re-evaluating the clinical trials.

## NEUROPHYSIOLOGY OF DEPENDENCE

The common denominator that unites all drugs of dependence is that they stimulate cells in the ventral tectal area (VTA) projecting to the NA to release dopamine (DA) – a crucial component of the body's pleasure mechanism ([Pierce and Kumaresan, 2006](#)), shown in [Figure 26.1](#). The NA is involved in learning and behaviour – inasmuch as any individual brain centre can be identified with a particular function. The VTA coordinates behaviour through its links to other limbic structures – such as the amygdala for motivation, hippocampus for memory and the NA for pleasure – and the prefrontal cortex for intention, personality and social acceptability. The NA is called the 'reward centre' and is central to reinforcement and conditioning. The intense 'high' induced by psychoactive drugs is associated with rapid and massive release of DA in the NA, well above normal physiological levels.



**Figure 26.1** Relationships of the 'reward' centre or mesolimbic circuit of drug reinforcement.

## Clinical points

DA release in the NA is a central mechanism in drug dependence.

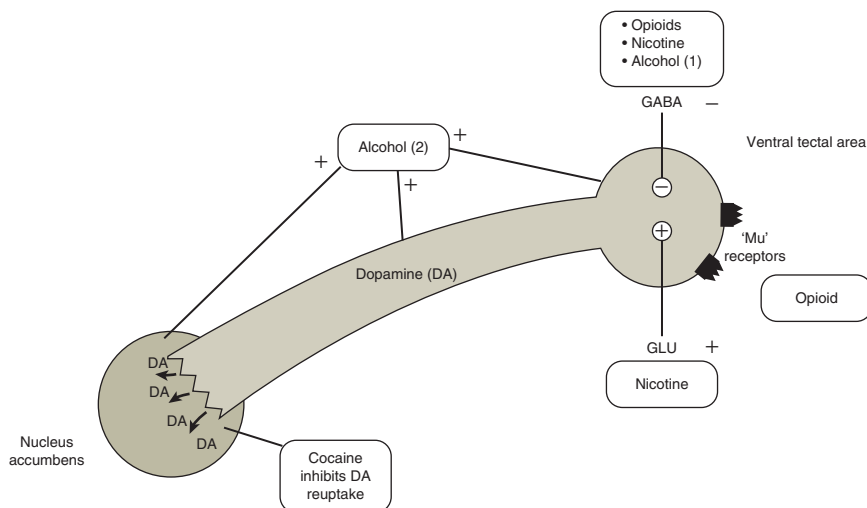
The neurophysiological details of the mechanism of this extracellular DA release are moderately well understood (Pierce and Kumaresan, 2006), represented in Figure 26.2. The DA release in the NA is proportional to opposing influences on the cell body within the VTA: essentially stimulated by glutamate and inhibited by gamma-aminobutyric acid (GABA). Opioids and nicotine reduce the activity of the GABA cells, thus disinhibiting DA release; nicotine may also increase glutamate activity. Ethanol has two dose-related effects, in opposite directions: small doses inhibit GABA pathways like opioids; higher concentrations suppress brain activity widely but also stimulate the body of DA cells directly. In contrast, cocaine blocks the reuptake of DA.

The mu opioid receptors are mainly responsible for the reinforcement properties of opioids: they are widespread on cell bodies in VTA and NA, though not on the actual cells that release DA. Dynorphin and the kappa receptor are also involved in the withdrawal syndrome.

Chronic excess of DA ends in down-regulation of DA receptors, which leads to both tolerance to drugs, and blunting of pleasure from other sources. Down-regulation is particularly associated with two transcription factors – cAMP responsive element binding (CREB) protein and delta-FosB. CREB is a relatively short-lived transcription factor that down-regulates DA receptors directly. Delta-FosB is relatively stable and can persist in the brain for weeks after the last drug exposure in established dependence and may be associated with craving. By regulating numerous genes it mediates the synaptic plasticity which contributes to various behavioural phenotypes in response to drug exposure, related to craving.

## POSSIBLE MECHANISMS OF ACUPUNCTURE

The NA, known to be central to drug dependence, has been shown by brain imaging studies in humans to be one of the limbic system centres whose activity is modified by acupuncture (Hui et al., 2005).



**Figure 26.2** Diagram of major mechanisms of drug stimulation of DA release in nucleus accumbens. DA, dopamine; GABA, gamma-aminobutyric acid inhibits; and GLU, glutamate stimulate release of DA. Alcohol (1), low dose; alcohol (2), high dose.

Han and colleagues in Beijing, who pioneered the discovery of endogenous opioid mechanisms in pain control by acupuncture, extended their work to the topic of opioid withdrawal, summarised in [Han et al. \(2011\)](#). Using a rat model, they found that EA at 100 Hz was more effective than 2 Hz for reducing most withdrawal symptoms, but the combination of 2/100 Hz for 30 min was optimal. The effect accumulated when treatment was repeated two to four times a day, and after a course of several days' treatment the effect lasted for 7 days. The superiority of 100 Hz suggests involvement of dynorphin and kappa receptors in the spinal cord, though the relevance of this in humans is unknown. Cui proposes that 100 Hz is better for physical aspects of dependence, and 2 Hz better for psychological aspects ([Cui et al., 2008](#)), though this could be an oversimplification.

### Clinical points

Repeated 2/100 Hz EA prolongs the suppression of withdrawal symptoms.

Several cellular mechanisms seem to be involved. The upregulation of the transcription factor CREB by repeated opioid administration is abolished by 100 Hz EA. Electron microscope studies have shown that 14 days of morphine administration induce swelling of the endoplasmic reticulum, blurring of membrane configuration and changes to structure of the myelin sheath of dopaminergic cells. These alterations are reversed by both 2 and 100 Hz EA ([Han et al., 2011](#)). Acupuncture also upregulates brain-derived neurotrophic factor (BDNF) levels in the VTA.

Other laboratories have confirmed the effects of EA in animal models. [Li et al. \(2011\)](#) found that a 20-minute session of 2 Hz EA at ST36 reduced alcohol self-administration in rats. A single session of high frequency (100 Hz) was ineffective, as was 2 Hz when given to the tail as sham control. Other groups found evidence of enkephalin release ([Liang et al., 2010](#)), which accumulates on repeated stimulation over three consecutive days.

[Yoon and colleagues \(2004\)](#) showed that 1 min's acupuncture with manual stimulation at HT7, traditionally used for mental disorders, inhibited DA release from the NA induced by ethanol, through suppression of GABA activity. Acupuncture to control points PC6 and on the tail had no effect. The same group subsequently showed that brief manual acupuncture (at HT7 but not at the control point, LI5) reduced morphine self-administration, again through GABA ([Yoon et al., 2010](#)).

Preclinical studies in humans support this evidence, using body points LI4 and PC8 in one arm, PC6 and TE5 in the other ([Han et al., 2011](#)). Han generally used adhesive electrodes in humans rather than needles, and a portable stimulation device (HANS), a treatment they called transcutaneous electrical acupuncture point stimulation (TEAS). During drug withdrawal, TEAS at 2/100 Hz rapidly reduced the increased heart rate, and subsequently reduced demand for buprenorphine substitution therapy.

Han's group also investigated the role of acupuncture in relapse prevention, using the laboratory model called conditioned place preference (CPP): offered two locations, an animal that has been rendered dependent by repeated doses of morphine spends more time in the location where the drug is available. The preference is abolished by naloxone, indicating the involvement of the mu opioid receptor. A single session of TEAS at 2 Hz suppressed CPP; 100 Hz needed repeated sessions to generate the effect, the delay presumably indicating the induction of gene expression ([Han et al., 2011](#)).

Both frequencies can achieve up to 35% reduction in DA release, and higher if repeated. In Han's hypothesis, a single dose of 100 Hz releases dynorphin (and its precursor, preprodynorphin) which inhibits DA release, and repeated doses induce gene expression. Han suggests that the DA system is sensitised by drug withdrawal, and desensitised by enkephalin induced by 2 Hz TEAS. Thus, 2 and 100 Hz have effects through different mechanisms.

Other researchers have addressed other potential mechanisms of acupuncture. Manual acupuncture at HT7 (but not ST36) reduced anxiety-like behaviour in a rat model of nicotine withdrawal, with associated reduction in corticotrophin releasing factor in the amygdala (Chae et al., 2007). Other groups report serotonin (5-hydroxytryptamine) release (Yoshimoto et al., 2006). Others have postulated a role for BDNF in this process (Chu et al., 2007).

While the full range of mechanisms of acupuncture for dependence is unknown, and their clinical relevance far from certain, there is sufficient evidence from laboratory research to support further research into clinical use, and even to suggest certain techniques for treatment.

## CLINICAL APPROACH

Acupuncture is used for drug dependence in a wide range of settings, mostly as an adjunct to other interventions and usually through practitioner enthusiasm, not formal health service policy. Enthusiasm is based on repeated observations that acupuncture given during withdrawal promotes relaxation and sleep, having a calming effect on people who are irritable and agitated, and reducing tension and anger so users participate in the programme. Acupuncture is also reported to help concentration and ability to cope. Patients who complain of sedation and lethargy during drug withdrawal feel more energetic and focussed after acupuncture. Patients also report reduced cravings, depression and pain. Acupuncture may be useful in combination with relaxation therapy, particularly for patients with dual diagnosis, drug dependence together with some other mental disorder (Stuyt, 2014; Stuyt and Mooker, 2006).

The type of personnel administering the acupuncture is variable: in some cases acupuncturists employed as staff of the treatment centre and in some cases existing staff (key workers, nurses, behaviourists, psychologists) are trained. One practitioner can treat a roomful of drug users simultaneously with great efficiency, and since needles are inexpensive, the overall treatment costs are minimal.

The maximum frequency of acupuncture used seems to be once daily for residential patients but usually only once or twice a week for non-residents. Few facilities have the resources to provide the theoretical optimal frequency of thrice daily in the acute withdrawal stage, and anyway local soreness in the ear points would be a hindrance.

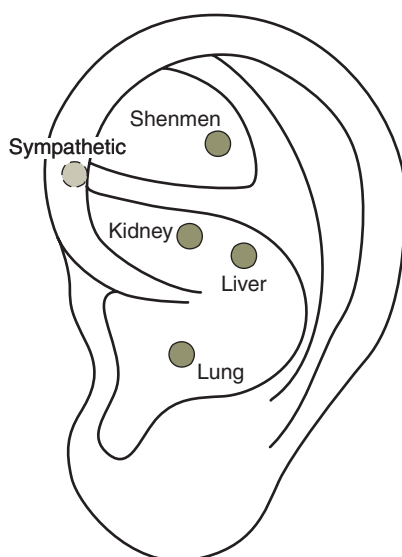
Treatment is usually auricular acupuncture according to the National Acupuncture Detoxification Association (NADA) protocol described later. Some acupuncturists also needle body points for particular symptoms, though points are effectively limited to hand and arm as patients remain fully clothed. It seems rare for EA to be used.

### Acupuncture techniques

Wen's original technique for opioid detoxification involved body and auricular EA, but in his subsequent clinical studies he used EA at 125 Hz to bilateral auricular Lung points for 30 min, twice a day (Wen and Teo, 1975).

Wen was visited in Hong Kong by Dr. Michael Smith, a psychiatrist, who introduced EA for drug dependence in Lincoln hospital in the Bronx, New York in about 1974. He gradually refined the treatment by increasing the number of auricular points used to five, and abandoning EA as unnecessary. In 1985, the NADA formed to promote the treatment and train practitioners in this standard approach (Brumbaugh, 1995).

**NADA protocol.** The NADA protocol is now widely used in treatment centres, outpatient departments, prisons – and many US clinical trials. Patients are needled at three to five points bilaterally (Fig. 26.3) with no needle stimulation. Treatment is the same for all drugs. Patients are typically seated in lounge chair and allowed to relax for 30–40 min before the needles are removed. Generally access is open on demand, and daily if desired. In some clinics, recovered patients have



**Figure 26.3** Points used in the NADA protocol.

themselves been trained to deliver the intervention which saves costs and may increase motivation. Acupuncture treatment is always linked to a treatment programme.

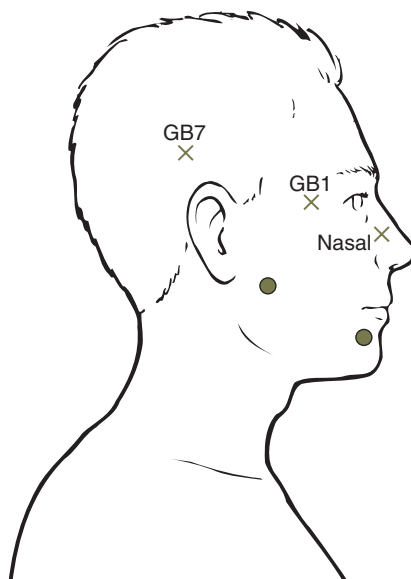
The NADA protocol is popular with staff and patients alike. Stuyt describes observation of effects in 367 inpatients with dual diagnosis (dependence and mental illness) after its introduction on a regular basis 5 days a week as part of a relaxation group, initially for tobacco dependence (Stuyt and Mooker, 2006). Patients who were agitated and irritable became calm; those who were lethargic became more energetic and focused; sleep and pain management improved; and those accepting acupuncture stayed an average of 70 days overall, compared with 39 for those who declined acupuncture.

**Body EA.** In China, use of EA in body points has dominated, using 'dense-dispersed' 2/100 Hz stimulation. Han typically uses rubber electrodes (TEAS) applied in two pairs: LI4 paired with PC8 on one side, and PC6 paired with TE5 on the other, at an intensity of twice the threshold for 30 min. In a sham-controlled study ( $n=55$ ), TEAS applied three times daily at maximum tolerable intensity for inpatients undergoing opioid withdrawal had a success rate at 14 days of 77% compared with 35% in the sham group (Meade et al., 2010).

The most intensive schedule for drug withdrawal that was identified in the available literature (Cui et al., 2008) recommended 2/100 Hz three times a day for 5 days, twice a day for 5 days, then once a day for 14 days. One session should be given on retiring to improve sleep.

The same schedule is recommended for relapse prevention. In a randomised clinical trial ( $n=154$ ), Han's group found TEAS self-administered up to three times daily was superior to usual care in maintaining abstinence: success rate was 44% in the TEAS group compared with 0% of the controls (Han et al., 2011).

**Other techniques.** Patterson developed her own version of electrostimulation to rubber electrodes fixed to the mastoid process and claimed specific frequencies were effective for different drugs (Patterson, 1976; Patterson et al., 1996).



**Figure 26.4** Face points used in some French studies of smoking cessation. Dots mark points used for sham acupuncture.

In France, a particular tradition has developed for treatment of smoking cessation using facial points (GB1, GB7) for smoking cessation, by manual stimulation only ([Lacroix and Besancon, 1977](#)) ([Fig. 26.4](#)).

A traditional Chinese approach claims to diagnose and treat the ‘underlying disorder’. One example of this applied to smoking cessation, a course of treatment was given without setting any quit date, allowing patients to quit in their own good time ([Steiner et al., 1982](#)). The study found no effect but was too small to be definitive.

**Repeating or prolonging the stimulation.** The effect of a single stimulation is short-lived. Some evidence supports daily repeats: out of 39 studies, 56% with daily stimulation were positive compared with 36% that used longer intervals ([White, 2013](#)). In outpatients when it is not possible to repeat the stimulation, indwelling needles (studs) or acupressure devices (*Vaccinia* seeds, or substitute beads) can be placed, usually at auricular points, for patients to stimulate when they feel withdrawal symptoms. This technique has been described for tobacco withdrawal symptoms.

The NADA technique does not involve indwelling studs or seeds, presumably for risk of contaminated needles falling out, loss to follow up and unpredictable behaviour.

Han has issued heroin-dependent patients with EA apparatus with rubber electrodes so that they can treat themselves repeatedly, initially three times a day ([Han et al., 2011](#)).

## Clinical research into acupuncture for dependence

Acupuncture for drug withdrawal is popular with patients and clinicians. The accumulated evidence from clinical trials – largely based on point theory – is not supportive. After describing the evidence, an attempt will be made to determine whether the studies might have failed to identify a real effect – because of, for example, inadequate treatment or poor choice of outcome measure.

## EARLY PROMISE

Four landmark early studies suggested that acupuncture alone as treatment for dependence had effects on abstinence.

Bullock and colleagues recruited 54 recidivist alcohol-dependent inpatients (with at least 20 admissions for alcohol; unemployed, and without personal support) for a sham-controlled RCT (Bullock et al., 1987). Three NADA ear points were compared to sham locations 5 mm away over 11 weeks. The verum group showed significantly lower attrition (37% vs. 7%) and fewer admissions.

This was supported by a second study ( $n=80$ ), similar but alternate allocation, not randomised. In the verum group, 21/40 completed the programme compared with 1/40 in the sham control group, and benefits persisted at 6 months (Bullock et al., 1989). All study personnel were blinded except the acupuncturist.

Lipton and colleagues randomised 192 participants dependent on cocaine (Lipton et al., 1994) to acupuncture (four NADA points) or sham (four auricular musculoskeletal points) for 1 month. The ratio of urines testing positive was significantly lower in the NADA point acupuncture group, although attendance rates did not differ.

In the fourth study, in 100 heroin-dependent patients, Washburn et al. (1993) found that the real acupuncture (NADA points) group adhered to treatment significantly better than the sham (nearby non-points) group over the 21 days of treatment (Washburn et al., 1993). There was a trend in favour of acupuncture for negative urines, 10% versus 4%.

In 2002, this initial promise was dramatically reversed by the publication of two large negative studies: 503 with alcohol dependence (Bullock et al., 2002) and 620 dependent on cocaine (Margolin et al., 2002), described in the relevant sections later. Since then, systematic reviews have summarised the evidence as 'equivocal' for alcohol (Cho and Whang, 2009), 'inconclusive' for auricular acupuncture for cocaine (Gates et al., 2006), 'inconclusive' again for opioid dependence (Lin et al., 2012) and 'no consistent, bias-free evidence' for smoking cessation (White et al., 2014).

## Acupuncture for alcohol dependence

### KEY CLINICAL TRIALS

Bullock and colleagues randomised 503 severely dependent people in a residential programme (Bullock et al., 2002) to four arms: no acupuncture; real acupuncture to four NADA points (located with a galvanometer); sham acupuncture at points 5 mm away; and personalised acupuncture according to symptoms. Treatment was given daily except Sundays, to a maximum of 18 sessions. The participants were predominantly white, mean age 38 years, and stayed an average of 5.7 days. There were no significant differences between groups.

One other study has a sample size over 100 and used body acupuncture (Toteva and Milanov, 1996). One hundred and ten participants were recruited after detoxification in Sofia Hospital, Bulgaria. Fifteen daily sessions of body acupuncture (selected from LI4, SL11, PC6, TE5, SI4, GB8, GB14, HT7, *Taiyang* and *Yintang*), and including EA for those more severely dependent, were compared with standard medical treatment with glucose, vitamins, benzodiazepines and propranolol. Acupuncture proved superior for the main outcomes: desire for alcohol, adherence to treatment, depression symptom scores and willingness for psychotherapy. There are no reliable long-term follow up data.

Rampes et al. revisited Wen's original work and tested ( $n=59$ ) the effect of six weekly EA (100 Hz) treatments at three NADA ear points for dependence, compared with EA to 'inappropriate' points (knee, internal secretion and elbow) and an untreated control group (Rampes et al., 1997). The main outcome, craving for alcohol, was significantly lower in both EA groups than the

controls at the end of treatment, though the difference did not persist to 24 weeks. There was no difference between effects of real and sham acupuncture.

## SYSTEMATIC REVIEW

Cho and Whang reviewed eleven studies on alcohol dependence comprising a total of 1110 participants (Cho and Whang, 2009). Only 2 of 11 trials reported all quality criteria satisfactorily. For alcohol craving, three out of four studies found acupuncture superior to no acupuncture. For completion rates, no differences were found, whether comparing acupuncture with sham acupuncture (risk ratio (RR)=1.07, 95% CI=0.91 to 1.25) or no acupuncture (RR=1.15, 95% CI=0.79 to 1.67). Only three RCTs reported acupuncture-related adverse events, which were mostly minimal.

The conclusions of the review were equivocal because of poor methodological quality and the limited number of trials.

## Acupuncture for cocaine dependence

### KEY CLINICAL TRIALS

Two large RCTs dominate the clinical evidence on acupuncture for cocaine, both testing the NADA point theory. In a three arm study, 236 participants enrolled on a residential programme were randomised to 28 treatments with real or nearby sham acupuncture or no acupuncture. Cravings were no different between the groups, and the acupuncture group had higher rates of positive urine tests (Bullock et al., 1999).

Margolin et al. (2002) recruited 620 participants with cocaine dependence, comparing NADA acupuncture with adjacent sham and with relaxation alone, daily over 8 weeks. There were no differences between the groups for retention in the study, positive urine tests, or abstinence.

A dose-response study compared the effect of daily, twice-weekly and once weekly NADA acupuncture in 202 outpatients. Although there was a trend in favour of daily treatment reducing cravings, there were no statistically significant differences (Bullock et al., 1999).

## SYSTEMATIC REVIEW

Seven studies with a total of 1433 participants were included in a Cochrane Review (Gates et al., 2006). Studies were of generally low methodological quality. For attrition, no differences between acupuncture and sham acupuncture were found: RR 1.05 (95% CI 0.89–1.23; four studies 556 participants). There was also no difference between acupuncture and no acupuncture: RR 1.06 (95% CI 0.90–1.26; two studies, 472 participants). No differences were found for any measure of use of cocaine or other drug.

However, the number of participants included in the meta-analyses was low, and power was limited. The review concluded: 'Moderate benefit or harm is not ruled out by these results'.

## Acupuncture for opioid dependence

Good quality clinical trials of acupuncture are scarce. Meade and colleagues randomised 48 patients undergoing standardised inpatient detoxification using buprenorphine-naloxone into a patient-blinded RCT (Meade et al., 2010). Electrical stimulation in the form of TEAS was given three times a day for 4 days, with one pair of electrodes attached to LI4 and the other side of the thenar eminence and one pair to PC6 and the opposite side of the wrist. Frequency alternated

between 2 and 100 Hz, and intensity was maximum tolerable. The sham group received current below the sensory threshold. Use of buprenorphine, the main outcome, was significantly lower in the verum group.

A review of 10 RCTs by [Lin et al. \(2012\)](#) included Chinese papers but not the above study of Meade et al. Four RCTs used auricular acupuncture, four used body acupuncture (mainly ST36, SP6, LI4 and PC6) with manual stimulation, and two used electrical stimulation (one with needles, one without). Courses of treatment lasted from 3 days to 6 months. The only two studies with reasonable reporting quality were both negative – but had sample sizes of only 60 ([Wells et al., 1995](#)) and 84 ([Bearn et al., 2009](#)): only large enough to identify effect size of 0.6 and therefore open to significant risk of type II error. Three of the four studies using auricular acupuncture found no benefit, but five using body acupuncture all reported some effect. One study that used HANS apparatus (as in the study by Meade et al.) reported a significant improvement in the severity of withdrawal syndrome. Another review examined the effect of acupuncture used as an adjunct to medication during the acute detoxification period ([Liu et al., 2009](#)). The majority of the studies were in Chinese, and of poor quality. The symptom scores were lower with acupuncture on several days out of the first 10. There was a trend to lower relapse rate at 6 months in the four studies with follow-up.

## Acupuncture for nicotine dependence

The Cochrane Review of acupuncture for smoking cessation (which also included acupressure, laser and electrotherapy) used Western and Chinese databases and assessed abstinence from smoking at two time-points: the earliest one after the end of treatment, to detect whether acupuncture had any effect at all; and at the last measurement up to 1 year, to detect an effect on sustained abstinence ([White et al., 2014](#)).

The evidence is extensive, old and contradictory. Comparing acupuncture with waiting list alone, three studies are not conclusive that acupuncture is superior. Compared with sham acupuncture, 16 studies with 19 comparisons produced a positive result at the early time point, with a RR of 1.22 (95% CI 1.08–1.38). The long-term result showed no effect, RR 1.10 (95% CI 0.86–1.40). This positive finding is unconvincing, being dependent on two individual positive studies which were quite different.

The studies are ordered in increasing sample size in [Figure 26.5](#), and it can be seen that the larger studies are more likely to be negative. Acupuncture was less effective than nicotine replacement therapy and no different from counselling and psychological approaches.

### Clinical points

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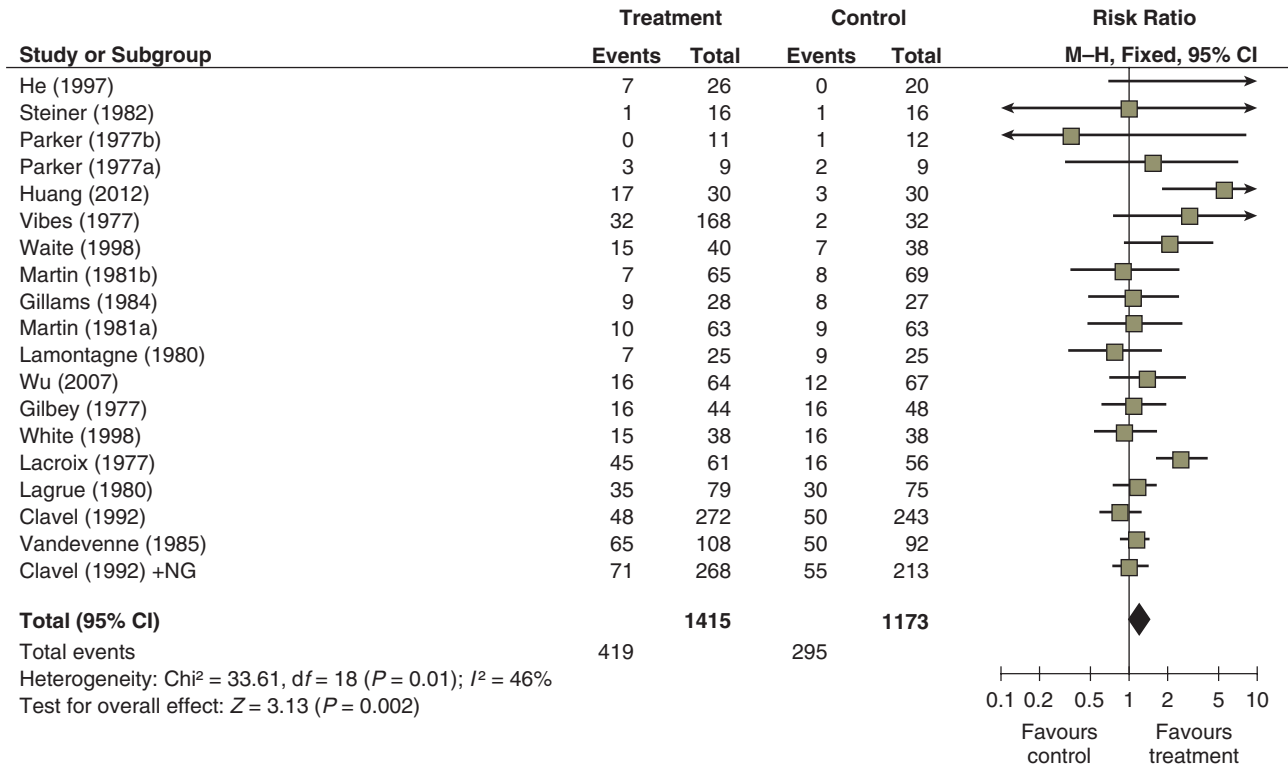
Evidence on acupuncture for smoking cessation is inconclusive, but moderate quality evidence suggests some techniques might be effective.

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One treatment technique appears promising: pooling all 14 studies that used continuous stimulation, whether acupuncture or acupressure, shows a positive effect of 1.69 (95% CI 1.32–2.16) compared with sham stimulation. This positive result was more marked for acupressure than for indwelling needles. There was no long-term effect shown, so the evidence remains inconclusive ([White et al., 2014](#)).

Three studies of acupressure gave a combined positive result, but short term only. Two studies of laser therapy produced opposite results, and six of cranial electrostimulation showed no effect compared with sham stimulation.

Putting all this evidence together, the reviewers concluded that the evidence is inconclusive on the effectiveness both of acupuncture and related techniques on smoking cessation. But in view of acupuncture's popularity, further studies are justified as long as they include some form of continuous stimulation.



**Figure 26.5** Meta-analysis of acupuncture versus sham acupuncture for smoking; short-term cessation. [Clavel \(1992\)](#), [Parker \(1977\)](#), and [Martin \(1981\)](#) have two comparison arms. (Reproduced from [White, A.R., Rampes, H., Liu, J.P., et al., 2014. Acupuncture and related interventions for smoking cessation. Cochrane Database Syst. Rev. 1. Art. No.: CD000009](#))

# Re-evaluating clinical trials of acupuncture for dependence

The positive experience with acupuncture described by patients and practitioners contrasts with the largely negative findings of clinical trials and systematic reviews, and in particular the strongly negative results of large, supposedly ‘definitive’, studies. In order to explore possible reasons for this paradox, details and results of all 48 suitable RCTs that are included in four systematic reviews were combined to see whether particular factors were more likely to be associated with positive outcomes (White, 2013). The review was exploratory and limited in several ways but suggests certain directions for of future research. Nearly half (23/48) RCTs had at least one outcome that was positive for acupuncture.

## Clinical points

23/48 RCTs of acupuncture for dependence have one positive outcome.

The success rates are not greatly different for the different drug classes, though decrease slightly in the order: opioids, cocaine, alcohol and nicotine. Success rates were 8/13 (62%) with body points, 2/5 (40%) using face points and 12/29 (41%) using auricular points. EA is more likely to be associated with positive outcomes (6/7, 86%) than manual acupuncture (17/41, 41%). The studies provided no conclusive information on the optimum number of needles but did suggest that bilateral needling was associated with greater effects on abstinence, craving and withdrawal symptoms.

## CHOICE OF CONTROL INTERVENTION

The major NADA studies compared acupuncture at the specific NADA points with nearby locations designated as inactive, or sham, ‘non-points’, which the neurological approach suggests would have similar activity unless sham points were on helix which has different innervation from the cavum (see Chapter 10). This issue was addressed in pilot studies in the 1990s: needling of NADA points in one ear was found to be more painful than needling off-point locations in the other ear (Margolin et al., 1993), and the helix was judged ‘least active’ (Margolin et al., 1995). Some studies used the helix as control site, though others simply used any point 5 mm away from the so-called ‘correct’ point.

The likely effectiveness of the control intervention undermines the findings of these sham-controlled studies based on NADA point theory, as reflected in the literature review. 75% (12/16) of the trials comparing acupuncture to non-acupuncture controls were positive, compared with 34% (11/32) of those comparing acupuncture with ‘sham’ needling techniques. This difference may of course be partly explained by the reduced expectations in groups with non-acupuncture controls.

## Clinical points

No point on the ear is likely to be inactive: the ear is not a suitable site for sham needle control.

## OUTCOMES

Long-term abstinence is the outcome that matters most in drug dependence, so naturally this was the outcome used in the majority (75%) of studies. However, patients talking about acupuncture usually emphasise its value during withdrawal – on symptoms such as craving, insomnia, anxiety and anger. The few studies that have evaluated this kind of symptom are more likely to be associated with positive results, that is, craving (9/16, 56% positive) and withdrawal symptoms (7/12, 58% positive) compared with abstinence (11/36, 31% positive) or attrition (5/16, 31% positive).

This all suggests that acupuncture should be tested for its effect on ‘softer’ outcomes reflecting comfort and easing of withdrawal, rather than simply measuring abstinence many months later.

## Clinical points

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Avoid unrealistic expectations of short courses of acupuncture when testing long-term abstinence.

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## FUTURE STUDIES

Some studies suggest future directions for research, such as an RCT ( $n=67$ ) in which veterans newly withdrawn from various drugs of dependence were randomised to twice-weekly NADA acupuncture, relaxation or usual care for 10 weeks. The primary outcome was craving, and secondary outcomes included anxiety and quality of life. Acupuncture was associated with significantly greater reduction of craving and anxiety scores than the usual care, similar to relaxation (Chang et al., 2010).

Acupuncture might make detoxification more bearable, and one benefit might be in attracting drug users into treatment – an outcome which has never been explored. The role of acupuncture in relapse prevention also needs exploring.

## Obesity

### INTRODUCTION

Obesity is a major global epidemic resulting from changes in food intake and exercise and has considerable consequences on health and life expectancy including increased incidence of insulin resistance, type II diabetes, dyslipidaemia, hypertension, some cancers, as well as osteoarthritis and sleep apnoea (Haslam and James, 2005). Effective management includes commitment to long-term weight reduction from permanent changes in diet, energy intake and activity. The role of short-term, stand-alone programmes of intensive weight loss, where acupuncture might have a role, should be seen in the overall context.

### POSSIBLE MECHANISMS OF ACUPUNCTURE

There is considerable evidence from laboratory studies that acupuncture activates mechanisms relevant to weight loss (Belivani et al., 2013). Obesity involves complex factors influencing the balance between anorexigenic and orexigenic neuropeptides in the hypothalamus; levels of beta-endorphin and serotonin release from neurones centrally; and in the periphery, opposing effects of the peptides leptin (derived from adipose tissue – reduces appetite) and ghrelin (derived from the stomach – blocks the effects of leptin). Moreover, obesity is associated with low grade inflammation.

Laboratory studies provide support for mechanisms of acupuncture, including influence on the activity of hypothalamic neuropeptides, leptin levels and inflammatory markers, and have frequently shown that acupuncture (mostly EA) may have a favourable influence on food intake and obesity, as well as on related outcomes including insulin resistance, lipid profile and inflammatory markers.

It is frequently stated that auricular acupuncture stimulates the afferent branch of the vagus nerve, whose efferent branch influences intestinal motility. This response has not been unequivocally established and is questionable since the afferent branch terminates in the descending trigeminal nucleus which is part of the somatic, not cranial, nervous system.

### CLINICAL APPROACH

The approaches used include regular body acupuncture (several times a week in Chinese clinics), with either manual or electrical stimulation; auricular acupuncture, usually with indwelling needles or beads, at various points including a supposed 'Hunger' point anterior to the tragus; and a combination of both.

Electrical stimulation is frequently used, though the optimal frequency is not known. Specially designed devices exist with metal or rubber electrodes to enable patients to self-treat transcutaneously. And in one review, the proportion of studies that are positive was higher with both EA (9/10) and manual acupuncture (6/7) than with auricular acupuncture (0/2) (Belivani et al., 2013).

One research group has shown effects in humans on body weight, leptin and ghrelin of manual (Güçel et al., 2012), electrical (Darbandi et al., 2013) and auricular (Abdi et al., 2012) acupuncture and auricular acupressure (Darbandi et al., 2012). In a four-arm study ( $n=80$ ), this group found no difference between effects of 6 weeks, twice-weekly body EA to abdominal and limb points and auricular acupressure, though both were superior to sham forms of each approach (Darbandi et al., 2014).

A different approach, more typical of Chinese clinics, consists of the ‘embedding’ of subcutaneous catgut suture(s) in the abdominal wall, left to dissolve over time. A review of Chinese studies (Liao et al., 2014) found it effective, but studies were not high quality and used a categorical measure (effectiveness rate) rather than mean weight change.

## CLINICAL EVIDENCE

Twenty-nine studies were reviewed by Cho et al. (2009) from searches of Chinese, Korean, Japanese and Western databases: twenty were individually positive. The ‘headline’ result of the meta-analyses showed a significant effect of acupuncture compared with lifestyle change, sham treatments, and conventional medication. Although the various meta-analyses against different control groups were positive, each included very few studies. The authors regarded the evidence as overall inconclusive because of low numbers and quality (two-thirds had a quality score of 1/5), but suggesting that acupuncture could have an effect on obesity.

Of the included trials, five had follow up periods of more than 8 weeks. The study ( $n=92$ ) with the longest follow up, 24 weeks, conducted in the US, found no difference in weight loss between daily self-acupressure at three points, qigong and self-directed support (Elder et al., 2007). Four studies followed up their participants for 12 weeks. Another from the US ( $n=96$ ) found auricular acupressure no different from sham point acupressure at the wrist (Allison et al., 1995). Four Chinese studies were positive: the first ( $n=120$ ) found body acupuncture on alternate days superior to diet alone (Mi, 2005); the second ( $n=160$ ) found manual body acupuncture two to four times per week combined with auricular acupressure more effective than waiting list (Sun and Xu, 1993); the third ( $n=150$ ) found manual body acupuncture on alternate days significantly superior to sibutramine (Nie et al., 2007); the fourth ( $n=161$ ) found acupuncture combined with auricular acupressure beads more effective than a Chinese herbal preparation (Li and Wu, 2006). The techniques used in the review (Cho et al., 2009) were so heterogeneous that it was impossible to make any suggestions whether one technique appeared most effective.

Since this review, several studies have shown positive effects of acupuncture compared with sham, up to 8 weeks. For example, Yeo et al. (2014) compared indwelling needles at five auricular points commonly used in Korean clinics with the single point Hunger and a sham consisting of inserting then removing the needle followed by placement of sham device. Weight loss was 6% in both acupuncture groups compared with 3% in the sham group. The evidence remains suggestive but not convincing.

## Concluding comments

Acupuncture is not a complete treatment for dependence but seems to have potential as an adjunct. Acupuncture is more likely to show an effect on withdrawal symptoms and craving than on long-term abstinence or attrition. Any acupuncture effect is likely to be relatively small and short-lived; for optimal effect, acupuncture may need to be repeated two to four times daily at the

start of treatment. There is no evidence of a point-specific effect of auricular acupuncture: one point is as good as another. Body acupuncture, sustained auricular stimulation, bilateral stimulation and EA should be explored further. Use of (non-invasive) rubber electrodes for repeated treatment is likely to be more acceptable than needles.

Acupuncture has known mechanisms that could be relevant to short-term weight loss. Although the balance of clinical trials is positive, there are few with sufficient long-term follow up to know whether acupuncture is a useful treatment for obesity in clinical practise.

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# Acupuncture for urogenital conditions

M. Pullman

## CHAPTER OUTLINE

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## Introduction

The chapter will describe the important advances and current understanding of neuro-uropsychophysiology and pathophysiology and relate them to acupuncture treatment. Medical acupuncturists who treat such conditions will find much to contemplate. A summary of the current nomenclature and clinical aspects of the urogenital diseases likely to be encountered will be included, as well as the key acupuncture research.

Urogenital disorders commonly produce symptoms of urgency with or without incontinence, urinary frequency and pain. These are symptoms that can be improved with acupuncture once serious treatable conditions such as infection and malignancy are excluded. Three conditions are most prevalent.

1. Bladder Pain Syndrome/Interstitial cystitis (BPS/IC), consisting of chronic (>6 months) pelvic pain, pressure or discomfort related to the bladder and associated with urinary symptoms such as urgency and frequency ([Hanno et al., 2010](#)).
2. Overactive Bladder (OAB) is defined as urinary urgency with or without urge incontinence, usually associated with frequency and nocturia and without pathology or urinary tract infection ([Abrams et al., 2002](#)).
3. Chronic Pelvic Pain Syndrome (CPPS) encompasses BPS/IC and Irritable Bowel Syndrome but also includes other pain syndromes affecting the pelvic cavity such as vulvodynia, orchialgia and chronic prostatitis in men.

These conditions all significantly interfere with quality of life. Conventional treatments are often of limited benefit, costly and frequently abandoned due to side effects.

Acupuncturists have long observed the benefits for patients of treating urogenital symptoms. In the past 30 years, urogynaecologists have been introducing sacral and peripheral nerve stimulation to treat urogenital conditions. These modern treatments have clearly evolved from acupuncture. The traditional acupuncture points used in treating these conditions, particularly SP6, BL28, BL32 and BL33, are the same points used in modern neuromodulatory approaches. In sacral neuromodulation (SNM), surgeons implant wires near the sacral nerve roots mainly at S3 and stimulate the ventral primary ramus with a constant low intensity stimulation (Siddiqui et al., 2010). In percutaneous tibial nerve stimulation (PTNS, aka posterior tibial nerve stimulation), needles or electrodes are placed at or around the SP6 acupuncture point (National Institute for Health and Excellence, 2010). Acupuncture can be described as an effective neuromodulatory technique. It has a role to play in a multidisciplinary approach to management of these conditions.

Acupuncture, SNM and PTNS have clinical effects that are being investigated with the benefit of new brain imaging techniques. An explosion of research and literature has added considerably to the treatment and understanding of chronic urogenital disease and yet there is still a great deal of uncertainty regarding aetiology and pathogenesis.

There is evidence accumulating that acupuncture may have significant clinical effects across a range of urogenital disease and can improve quality of life. The urgent challenge remains for acupuncture to become more widely accepted and included early in management of these conditions. Acupuncture should be considered before any major surgery is contemplated for pain or symptom control.

## Neuro-uropsychology

Sensory information from the lower urinary tract (LUT) is transmitted to the lumbosacral spinal cord via afferent axons in the pelvic (S2–4), pudendal (S2–4) and hypogastric (T11–L2) nerves. Convergence of sensory information from other pelvic structures such as the colon occurs in the dorsal horns at these spinal segmental levels, as well as in supraspinal regions. This is the likely mechanism for the close correspondence between bowel and LUT disorders (Rouzade-Dominguez et al., 2003).

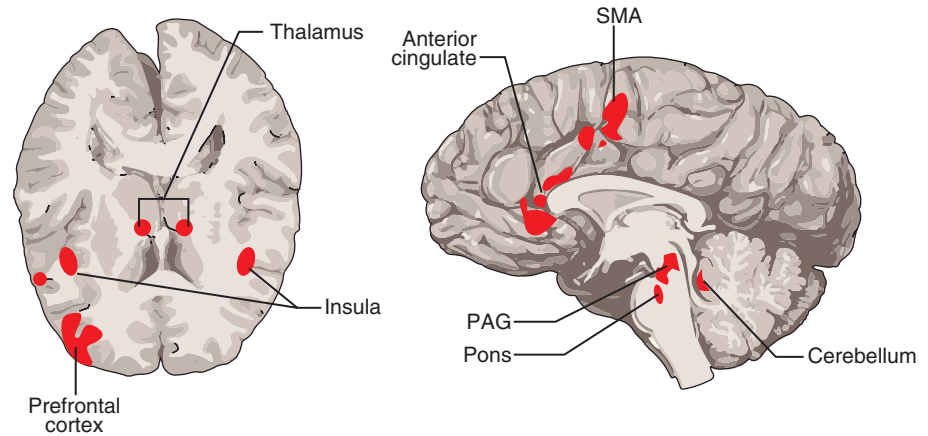
Point selection using a segmental approach (e.g. needling S2–S4 dermatomes/myotomes) has become the mainstay of acupuncture treatments.

## MICTURITION – PHYSIOLOGY AND PATHOPHYSIOLOGY

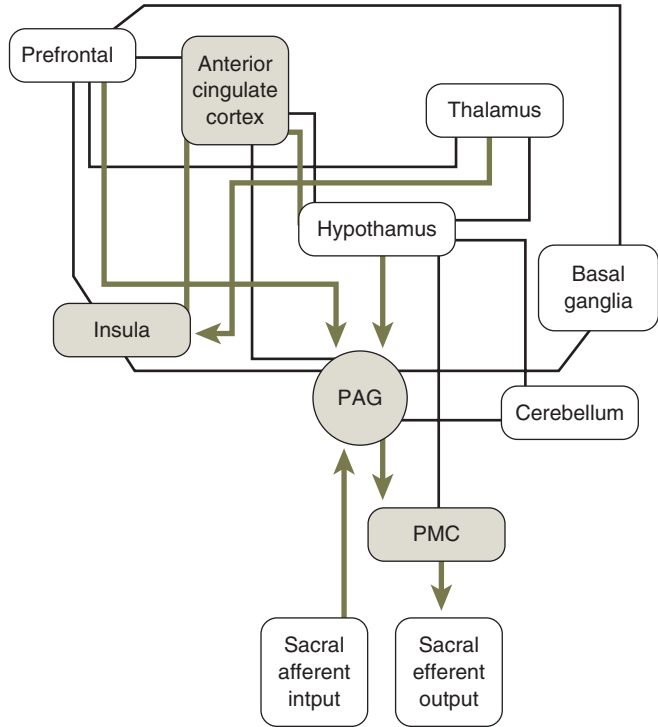
In simple terms micturition is organised in two phases, storage and voiding. During storage (99.7% of 24 h period), the sympathetic outflow maintains detrusor muscle relaxation and continence. Activation of the S2–4 parasympathetic outflow produces contraction of the smooth detrusor muscle and relaxation of the striated internal sphincter to allow voiding in response to bladder filling (typically 5–8 times a day).

Urinary physiology in normal function involves mechanoreceptive A delta and nociceptive C fibres relaying from the bladder to the sacral spinal cord. It is believed that in a normal LUT, the C fibres have little role to play but may become sensitised in disease or injury.

The last 10 years have seen a dramatic increase in research, both in attempting to elucidate the pathophysiology of bladder conditions and to test various neuromodulatory techniques used in treatment. This has culminated in the proposal of a 'Brain Bladder Control Matrix', a concept based on a review of 24 papers from the late 1990s, using single photon computerised tomography (SPECT), positive emission tomography (PET) and functional magnetic resonance imaging (fMRI) (Kavia et al., 2005). The review has been summarised by Fowler and Griffiths (2010) and is recommended reading for any medical acupuncturist treating patients with these conditions (Figs. 27.1 and 27.2).



**Figure 27.1** Brain areas involved in the regulation of urine storage. The thalamus, insula, prefrontal cortex, anterior cingulate, periaqueductal grey (PAG), pons, medulla and supplementary motor area (SMA) are involved in the regulation of urine storage. (Reproduced from Fowler, C.J., Griffiths, D., de Groat, W.C., 2008. *The neural control of micturition*. *Nat. Rev. Neurosci.* 9 (6), 453–466 with permission of the publisher.)



**Figure 27.2** Probable intracranial circuits for bladder control. Probable connections between forebrain and brainstem structures that are involved in the control of the bladder and the sphincter in humans. Arrows show probable directions of connectivity but do not preclude connections in the opposite direction. In spite of this complexity, the pontine micturition centre (PMC) remains the origin of the final common pathway, from brain to spinal cord. (Reproduced from Fowler, C.J., Griffiths, D., de Groat, W.C., 2008. *The neural control of micturition*. *Nat. Rev. Neurosci.* 9 (6), 453–466 with permission of the publisher.)

The midbrain periaqueductal grey (PAG) receives information from the bladder directly via sacral afferents and has been shown in neuroimaging studies to be activated during bladder filling (Griffiths et al., 2005; Athwal et al., 2001; Matsura et al., 2002). The PAG is under the strong influence of other regions especially the prefrontal cortex (PFC) and limbic system. These higher brain regions influence the basic reflex system thus allowing the person to choose when and where is the most appropriate place to allow micturition.

The limbic system is particularly concerned with emotion, memory and attitude and is the site for the affective component of pain perception in the brain. It consists of a number of structures, including the insula (an island of cortex deep to the lateral sulcus that separates the temporal and fronto-parietal cortices) and the anterior cingulate cortex (ACC – the frontal part of the cingulate cortex on the medial surface of each cerebral hemisphere which form a collar around the corpus callosum), and it is regarded as the most important area for ‘sensing’ the physiological condition of the patient.

Interestingly the afferent input to the insula is through small diameter (Aδ and C) fibres, entering through lamina 1 of the spinal cord, for example bladder afferents. Acupuncture also stimulates Aδ fibres that presumably therefore also could influence the insula. This has been suggested by Napadow’s work on fMRI responses to acupuncture in this area (2005) and PET scans (Pariente et al., 2005).

The limbic system is closely linked to the PFC, thus completing the complex supraspinal circuitry involved in bladder control. The PFC is probably the main candidate amongst all the above for final control over voluntary voiding. Lesions in the PFC can cause frequency, urgency and/or retention (Andrew and Nathan, 1964).

The PAG therefore acts as the signal processor that activates or suppresses another nearby area in the pons, the pontine micturition centre (PMC). In the storage phase, the PAG suppresses the PMC. When this suppression is reduced, the PMC transmits efferent signals to the bladder via the sacral spinal cord to achieve voiding.

Greatly increased activation of the insula has been shown in patients with OAB on bladder filling as compared with controls (Griffiths et al., 2005). This indicates a role of the insula in sensing bladder distension.

It is thought that abnormal responses or subtle lesions in the insula and medial PFC could dramatically affect LUT function and therefore have a role in the aetiology of urogenital disorders. Patients often exhibit strong negative emotional responses that may produce conditioning and deterioration in their LUT symptoms. The interference with the suppressive role of the PAG generates symptoms of frequency and nocturia of low volumes.

### Clinical points

Prefrontal cortex (PFC) and insula are closely involved in bladder control, and are known to be modulated by acupuncture.

Another interesting observation involves patients with BPS/IC undergoing cystoscopy and distension under general anaesthetic. These patients often exhibit hypertension and tachycardia in response to minimal stretching of the bladder. The response suggests a significant degree of central sympathetic hyperactivity. Acupuncture can modulate the default mode network and the sensorimotor network in the brain (Dhond et al., 2008) decreasing sympathetic tone. This could provide another explanation for the observed clinical effects of acupuncture. Patients with this response could possibly be selected for acupuncture. Further research is warranted in this area.

### Clinical practice

Three main conditions – OAB, BPS/IC and CPPS – are commonly encountered by the acupuncturist. In the author’s experience there is much overlap. The terminology is confusing and still evolving. The symptoms are the key to the diagnostic category.

Many of the early acupuncture studies observed patients with so-called irritative bladder symptoms (frequency, nocturia, urgency with or without urge incontinence). The evidence from many of these studies suggested LUT symptoms and quality of life scores improved.

A common factor in the positive studies of acupuncture for bladder dysfunction appears to be either manual or electrical stimulation at SP6, BL33 and BL28 or combinations thereof. These points are effectively accessing the sacral nerve roots. SP6 stimulates the S2 myotome via flexor digitorum longus or the posterior tibial nerve at the ankle whereas BL28 lies at the level of the posterior S2 foramina. In SNM and many animal studies, the S2 nerve root is often the one of choice (effectively BL32).

Segmental acupuncture at BL23, CV4 and CV6 will send afferent impulses to the lower thoracic and upper lumbar spinal cord. Sympathetic outflow from these levels theoretically should facilitate bladder filling and decrease frequency of micturition. In clinical practice, however, autonomic modulation cannot be predicted simply by which segmental levels are stimulated.

SNM is being used increasingly with success in conditions such as idiopathic voiding dysfunction (Fowlers Syndrome) and intractable urge incontinence. Attempts to find predictive factors for success in SNM have however largely failed (Scheepeens et al., 2002). Tom et al. (2011) found that psychological screening failed to predict response to SNM other than to show higher risk of adverse events.

## Overactive bladder

This common and debilitating condition is a considerable burden both to the patient and to healthcare budgets (Marinkovic et al., 2012). Patients can complain of nocturia in excess of 10 times per night. Daytime frequency means that travelling more than the shortest distance involves the logistical nightmare of constantly seeking out public conveniences.

It is estimated that there are 54 new cases of OAB per 1000 women per year in the West, with an overall prevalence of 16.9%. Approximately 11–16 million women are affected in the US (Agency for Healthcare Research and Quality (AHRQ), 2009). In the US in 2009, it was estimated that the disease specific expenditure for OAB was \$24.9 billion (£16 billion) (Onukwughu et al., 2009). Numerous studies have indicated that OAB is associated with lower quality of life scores than many other chronic conditions including depression, asthma and diabetes. Many patients go untreated or fail to seek help. There is also evidence to suggest that there are many surgical and medical consequences of OAB induced nocturia such as falls at night resulting in injuries, for example fractured neck of femur. Depression is also common in OAB sufferers. Hence the burden to health care systems may be even greater than estimated (Wagg et al., 2007). It has a strong association with other chronic conditions for which acupuncture treatment may be sought, such as irritable bowel syndrome, fibromyalgia and chronic fatigue. It can be a lifelong disease.

OAB is most common in patients over 40 years old. One study suggests that 60% of older or disabled patients seek treatment yet only 27% receive it. Patients have often suffered with urinary symptoms for many years prior to presentation. It seems to be a silent epidemic.

The aetiology of OAB is largely unknown. Only about 50% of OAB patients have evidence of detrusor instability. The causes are probably multifactorial involving one or all components of the micturition cycle. The bladder muscle itself may exhibit increased excitability and therefore stimulates afferent nerves before the bladder is full. Another possible mechanism in patients with OAB syndrome is abnormally high afferent processing in supraspinal or spinal areas related to bladder filling, i.e. 'wind-up'.

## CLINICAL APPROACH

OAB is a clinical diagnosis that relies on history of urgency, frequency (>8 voids per day) or nocturia (2 or more voids after falling asleep, with sleep between voids). Urge incontinence may or may not be present. Treatable causes must be sought such as diabetes, drugs, bladder calculi,

infection or tumour. Urine analysis and cytology should be performed and voiding diaries commenced. , [National Institute for Health and Clinical Excellence \(2006\)](#) guidelines suggest which patients to refer for specialist care. These include patients with

- macroscopic haematuria
- microscopic haematuria in over 50s
- recurrent urinary tract infection and macroscopic haematuria in over 40s
- suspected malignant genitourinary mass.

Conventional treatment is effectively a two-part process ([Thüroff et al., 2011](#)). It is important to mention here that a placebo response in the range of 33–56% has been generally reported in the literature for OAB across a wide range of treatments. First line management involves dietary modification, bladder training, biofeedback and anticholinergic drugs. Patients are encouraged to lose weight, drink less caffeine and rationalise their fluid intake. Anticholinergic drugs are the mainstay of medical management. They compete with acetylcholine, inhibiting its effect on detrusor muscle contraction and possibly directly decreasing bladder afferent activity. Despite reasonable evidence for efficacy and low cost (approximately £400 for a year's supply), compliance is poor with only 50% still taking drugs at 6 months ([Basra et al., 2008](#); [Gopal et al., 2008](#)). Side effects can add to the poor quality of life already being suffered by OAB patients. The elderly are particularly at risk of central nervous system toxicity such as confusion, dizziness and somnolence. Acupuncture could be offered as part of a first line package particularly if there are contraindications to anticholinergic drugs.

## EVIDENCE

In 2009 the Agency for Health and Research Quality (AHRQ) Evidence Report 187 looked at evidence for all treatments from 1966 to 2008 in management of OAB. The report reviewed 232 publications of which only 20 were good quality. They concluded that there was lack of high quality evidence to support clinical decision making across all modalities. There was insufficient evidence to support definitive choice of acupuncture as a treatment option, but it promises modest improvements in quality of life and cystometric filling, similar to that reported in many drug trials. This conclusion was based on one study by [Emmons and Otto \(2005\)](#) in which 85 patients were randomised to four 20 min sessions of manual acupuncture at SP6, BL39, BL28 and CV4. The control group were given penetrating sham acupuncture at GB31, ST36, BL12 and CV12. These patients all had symptoms of urge incontinence, frequency and urgency. Results confirmed that incontinent episodes were reduced by 59% compared to 40% in the control group, although this difference was not significant. There were also smaller percentage changes in bladder capacity, urgency and frequency. Scores on the Urinary Distress Inventory and Incontinence Impact Questionnaire were improved in both groups with the difference between the two groups being statistically significant.

In a non-randomised study, [Pigne et al. \(1985\)](#) showed cystometric improvements and decreased frequency in 16 OAB patients. [Philip et al. \(1988\)](#) showed subjective, symptomatic improvements in 10 out of 13 patients with detrusor instability. There was no cystometric confirmation of these findings. Notably, 10–12 weekly sessions were given in this study. [Chang \(1988\)](#) gave acupuncture at SP6 alone, finding 22/26 women had subjective improvement compared to 6/26 in the control group in whom ST36 was used. Also there were improved cystometric capacities in the SP6 group.

[Kelleher et al. \(1994\)](#) were the first to compare acupuncture with conventional treatment. In a prospective randomised controlled trial of 39 women, the effect of acupuncture was shown to be no different from that of anticholinergic drugs for treatment of irritative bladder with good compliance and better side effect profile. Again SP6, BL23–28 were used together with two more lumbar paravertebral points. Urgency and frequency were improved in both groups and nocturia only in the acupuncture group.

Excellent evidence exists for the use of posterior nerve stimulation (PTNS) i.e. electrical stimulation applied to a needle in the region of SP6. It also appears that 12 weekly sessions has been adopted as standard in most PTNS studies. This has not been compared to shorter and therefore cheaper regimes.

Historically, PTNS has been used by urogynaecologists from as early as 1987. The SUMIT trial (Peters et al., 2010) is a multicentre study that assessed the efficacy of PTNS against sham stimulation. In this study 220 patients were randomised to PTNS or sham therapy, which included use of the non-penetrating Streitberger needle at the same site as the PTNS. The site used for PTNS, approximately 5 cm cephalad to the medial malleolus, is very close to the acupuncture point SP6. The 34g needle was placed at a 60° angle and the stimulator set at 20 Hz with a current level 0.5–9 mA. Twelve, 30 min, consecutive weekly sessions were carried out. At 13 weeks, individual global response assessments for overall urinary symptoms showed statistically significant improvement with 54% reporting markedly or moderately improved responses compared to 20.9% in control group. Frequency, night-time voids and urgency all improved in the active group compared to sham. Subjects failed to differentiate between the active and control intervention. This was the first PTNS study to use the Streitberger needle (a blunt telescopic needle that is intended to be non-penetrating). The group claimed that this provided level 1 evidence that PTNS is safe and effective in improving OAB and that PTNS is a viable treatment for OAB.

### Clinical points

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Percutaneous nerve stimulation is similar to EA at SP6 and offers proven benefits for OAB.

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The OrBIT trial (Peters Macdiarmid et al., 2009) showed that 12 weekly PTNS were comparable to anticholinergic treatment in treating OAB and that sustained improvements at 1 year were present with periodic treatments in 96% of the 12-week responders.

SNM has been introduced into treatment algorithms with a quoted success rate of around 50% in OAB with urge incontinence. It is now supported by level 1 evidence in women. Reported long-term data show a favourable outcome, with success in up to 84% with urge urinary incontinence 5 years after implantation (Van Kerrebroeck et al., 2007).

SNM, however, is a costly treatment. The implanted hardware alone costs ≈£8400 and a battery replacement will cost ≈£5300. Additional costs include the test procedure (traditional or two-stage nerve evaluation), and surgical revisions (excluding battery replacements) are required in up to 48% of patients during a 5-year follow-up period. No recent cost-benefit analysis has been reported for SNM in relation to urological indications.

These studies are important for acupuncturists especially those concerning PTNS, which is quite similar to electroacupuncture at SP6 (Moossdorff-Steinhauser and Berghmans, 2013). Another important factor to take into consideration is that in studies to date only about 50% of patients prescribed anticholinergic drugs for OAB are still taking them at 6 months. In 2000 \$1 billion was spent on drug treatment for OAB. This was despite significant non-compliance. Neuromodulation with acupuncture or PTNS may have a significant role to play in the management of this group.

## Bladder pain syndrome/interstitial cystitis

BPS/IC has a prevalence of about 300 per 100 000 in women with, and 10–20% of that figure in men. It is associated with IBS and fibromyalgia and these conditions may have a common biochemical or genetic defect. Adult female first-degree relatives of patients with BPS may have a prevalence of BPS 17 times that of general population. Its aetiology is unknown, and there is no histology pathognomonic of the syndrome. Putative theories suggest that an initial bladder insult from infection, trauma, autoimmune disorder, bladder over distension, etc. may result in the development of damage to bladder interstitium with increased intracellular ATP release.

Increased afferent nerve sensitivity could cause spinal cord changes and development of a neuropathic bladder. Psychological neuropathology may also have a role. The incidence of sexual or physical abuse is higher than unaffected controls.

BPS/IC is a diagnosis of exclusion. The evidence to date does not lend itself to formulating a treatment plan.

The patient with BPS/IC commonly embarks on a lifelong journey of various treatment options balancing symptomatic relief against side effects, cost or inconvenience. Explanation and education of a chronic pain condition is extremely important. Dietary advice to reduce citrus fruits, spicy foods, alcohol and caffeine can be helpful to individuals. Simple analgesics and intravesical agents are often used as first line. Amitriptyline may help and is supported by level 1b evidence (van Ophoven *et al.*, 2004; van Ophoven and Hertle, 2005). In some, augmentation cystoplasty and urinary diversion with or without cystectomy is the only option left. This is a major procedure with significant morbidity.

Reeves and Pullman (2009) reported a case series where 6 weekly sessions of acupuncture were carried out on 15 patients diagnosed with BPS/IC by a consultant urogynaecologist. Fourteen patients had tried at least one treatment prior to acupuncture. Eleven patients had tried intravesical agents with no success. Four patients had unsuccessfully tried gabapentin. Points used were SP6, BL28, BL33, BL23 and LR3. All patients experienced a significant improvement in symptoms and quality of life. This was defined as a >50% improvement in MYMOP scores (measure yourself medical outcome profile). The authors reported that the nature of the clinic where time is allowed for discussion and relaxation undoubtedly had an impact on the outcomes as revealed in subjective data obtained from patient feedback.

Other acupuncture studies already cited in the text in treatment of OAB can be used as evidence that symptomatic control of LUT can be achieved in some patients BPS/IC. Some patients with BPS/IC exhibit significant tenderness over the sacroiliac joints. Whether this has a role in the condition is debatable but is an indication to needle the area.

The goal of treatment in BPS/IC is undoubtedly to maximise quality of life. These patients ideally should be assessed by a urogynaecologist experienced in BPS/IC before acupuncture. Ineffective treatments should be discontinued. The patient must be encouraged with a positive but realistic attitude. The approach taken in the author's clinic is to emphasise the increased mood, better sleep and gradual reduction in pain that can be achieved with acupuncture. No change is made to the patient's on-going treatment but acupuncture often improves the patient's confidence enough to gradually allow them to reduce medication or increase the intervals between intravesical instillations. Acupuncture in some cases appears to act synergistically with existing treatments such as amitriptyline.

## Chronic pelvic pain syndrome

This chronic pain syndrome encompasses orchialgia, chronic prostatitis (CP/CPSP) and vulvodynia.

CP/CPSP is common with prevalence about 10% in the community. Only about 10% have a treatable infectious cause. The other 90% experience a debilitating chronic perineal/pelvic pain associated with LUT symptoms and/or sexual dysfunction for at least three of the previous 6 months. A recent review suggests moderate improvement over placebo for alpha blockers, antibiotics and anti-inflammatories (Anothaisintawee *et al.*, 2011). This was particularly so for secondary outcomes regarding quality of life. Acupuncture was not mentioned as an option in this review. However, there have been some interesting acupuncture studies in this area.

Chen and Nickel (2003) treated 12 men who were given 12 sessions of acupuncture over 6 weeks. Points used included BL10, BL28, BL23, BL54, BL35 CV4, CV3 and SP6. Electroacupuncture was used at 20Hz on the CV points and iliohypogastric and ilioinguinal

nerves. Ten patients (83%) had a sustained greater than 50% decrease in the National Institutes for Health-Chronic Prostatitis Symptom index (NIH-CPSI). No adverse effects were reported.

In an RCT in 89 men with CPPS, [Lee et al. \(2008\)](#) showed that after 20 sessions, acupuncture proved nearly twice as likely (73%) to improve CP/CPPS symptoms over sham treatment (47%). Those completing acupuncture had a 2.5 fold likelihood of experiencing long-term benefit (32%) compared with sham (13%).

[Lee and Lee \(2009\)](#) investigated the clinical effect of EA at 4 Hz (5–10 mA) to bilateral BL32, BL33 and GB30 (70 mm needles to reach piriformis). This was compared to a sham acupuncture group and also to an advice and exercise group in a total of 63 men. Twelve sessions of acupuncture were carried out over 6 weeks. At 6 weeks the NIH-CPSI had decreased significantly in the EA group compared with the other groups, and the mean prostaglandin level in the postmassage urine also significantly decreased.

## Vulvodynia

Vulvodynia is a chronic vulval pain or burning sensation for over 3 months without an obvious lesion. The pain may be localised or generalised and provoked or spontaneous. A study from the US suggested that up to 16% of women have experienced chronic vulval pain at some time in their lives with 7% prevalence. The aetiology is unknown but may be related to infection, inflammation or tumour, all of which must be excluded. Any patient with vulvodynia considering acupuncture must be assessed by an experienced dermatologist or urogynaecologist. A full sexual history must be taken as associated sexual dysfunction is common and may need follow-up with psychosexual counselling. Amitriptyline and gabapentin have a role in the treatment of unprovoked vulvodynia but have limited evidence base and low compliance after 3 months.

[The British Association of Sexual Health and HIV \(Clinical Effectiveness Group\) \(2014\)](#) recommended that acupuncture be offered in the treatment of unprovoked vulvodynia. This was based on a case series of 12 patients ([Powell and Wojnarowska, 1999](#)). Five of these patients improved significantly and wished to continue treatment. Four of the remaining seven patients felt acupuncture was more effective than any other treatment. Only four points were used (SP6, SP9, LI4 and LR3) and treatment given for five sessions.

[Danielson et al. \(2001\)](#) reported a case series of 14 women with provoked vulvodynia or vulvar vestibulitis. Manual acupuncture was given 10 times. Points used included CV4, CV6, SP9, GV3, BL31 and LR8. Needles were left in 30–45 min. Three months after the last acupuncture session 10 out of the 13 who completed the study still recorded their negative QoL factors as less pronounced than at baseline.

Unpublished data (author's own study) showed that 9 out of 15 women referred from a specialist vulval clinic and treated with acupuncture had a positive outcome based on symptom scores and comments. Manual acupuncture was given at four sacral points, LR3 and SP6, and needles were left for 15 min. Five of the women were deemed sufficiently relieved of symptoms to be discharged from clinic. Six out of the fifteen women had a greater than 50% improvement in their primary symptom. Five women reported no effect.

## Myofascial pain and CPPS

There are many causes of CPPS including visceral pain, adhesions, endometriosis, pelvic congestion, primary and secondary dysmenorrhea, gastroenterological and urological conditions. Often no definitive cause can be found. Myofascial pain syndrome can cause, or exacerbate, pelvic pain and must always be considered.

[Slocumb \(1984\)](#) noted myofascial trigger points (MTTrPs) in 89% of women presenting with CPPS, regardless of the underlying pathology.

Trigger points in any fascia or muscle innervated by T12 – L4 spinal segments can cause referred myofascial pain (dull, aching and diffuse) to the pelvis. Muscles particularly implicated are iliopsoas, quadratus lumborum and piriformis. The segments T10–S4 similarly innervate the pelvic organs. The back, buttock and abdominal musculature should be carefully assessed for MTrPs and tender areas in all patients presenting with CPPS.

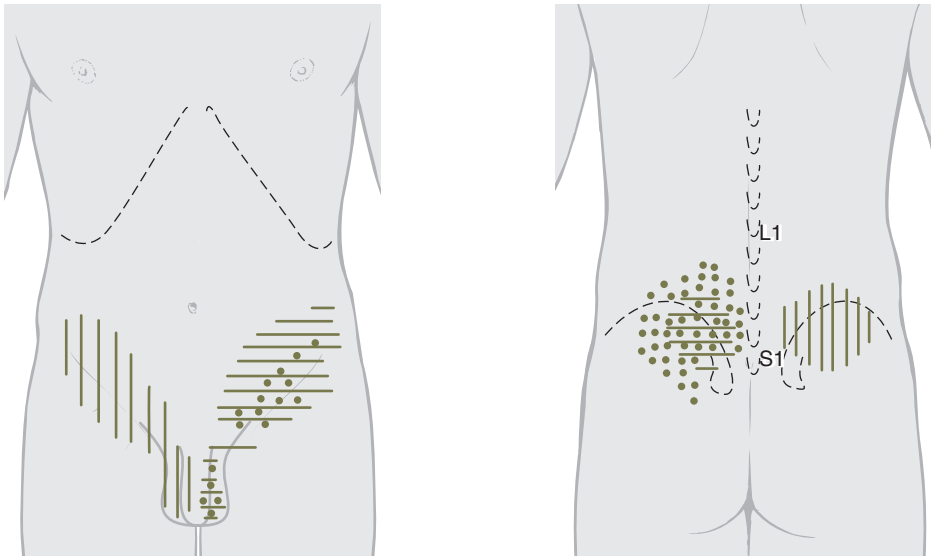
Trigger points in levator ani, coccygeus, piriformis and gluteus maximus are also important treatable causes of CPPS. If a patient presents with perineal pain that is almost exclusively worsened by sitting and at other times is diffuse throughout pelvis and lower abdomen, then examination of the perineum looking for MTrPs is recommended. Two of the most dramatic cases I have witnessed were in men, both in their 70s who had a history of this nature for more than 5 years, both following endoscopic prostate surgery. Neither man could sit for longer than 10–15 min without getting the sensation of ‘sitting on a golf ball’. They both had a trigger point in the perineum, probably levator ani. One was cured with one needle, and the other took three sessions of acupuncture before also getting complete relief. Acupuncture was carried out in the left lateral position after cleaning the perineum with a sterile wipe. No adverse effects were observed, and it was well tolerated by the patients.

### Clinical points

MTrPs may cause symptoms similar to CPPS.

Scrotal pain can be caused by referred pain from trigger points in external oblique just above the inguinal ligament; or in the adductor longus muscle near its insertion to the pelvic bone. Kellgren (1939) showed that this pain could also be referred from muscles supplied by L1 (Fig. 27.3).

Needless to say, examination of the perineum and even of rectum, when indicated, can be difficult to carry out in an acupuncture clinic. However, with appropriate care and effort such as the presence of a chaperone this can be achievable. Education of GPs and urogynaecologists to consider myofascial pain syndrome and to perform acupuncture should be encouraged.



**Figure 27.3** Distribution of pain from testis (vertical hatching) and muscle supplied by first lumbar segment (abdominal obliques, horizontal hatching, multifidus, stippling). (Reproduced from Kellgren, J.H., 1939. On the distribution of referred pain arising from deep somatic structures with charts of segmental pain areas. *Clin. Sci.* 4, 35–46.)

From clinical experience, Felix Mann describes points at the anterior superior iliac spine area that can be useful in patients with urogenital disease. Periosteal pecking at this point may produce strong sensations.

## Mechanisms of acupuncture in urogenital disease

Afferent information from the major pelvic organs such as the bladder is conducted through the hypogastric, splanchnic, pelvic and pudendal nerves to cell bodies in the thoracolumbar and lumbosacral dorsal root ganglia. In disease, for example IC/BPS, strong or noxious prodromic (peripheral to central) afferent stimulation can lead to antidromic (central to peripheral) sensitisation of a myotome or dermatome. This leads to somatovisceral and viscerosomatic reflexes. Whether this explains the exquisite tenderness of SP6 in many patients with bladder disease is still a mystery but may explain the significant number of trigger points in these patients (see previous section) (see also [Chapters 3 and 6](#)).

Of the many animal studies reported, [Wang et al. \(2012\)](#) performed an elaborate and interesting study on 55 urethane anaesthetised rats investigating the effects of stimulation at BL33 on bladder activity and bladder related neurons in and around the pontine region known as 'Barrington's' nucleus (equivalent to the PMC in humans). Their findings are fascinating and may stimulate further research.

1. Acupuncture suppressed bladder activity, in a segmentally specific manner.
2. Acupuncture altered the firing profiles of the neurons around Barrington's nucleus before the suppression of bladder activity.
3. The acupuncture effect was possibly mediated through GABAergic receptor systems.

These findings suggest the possibility that the acupuncture effect on bladder function is mediated through supraspinal regions, especially the PMC.

[Hino et al. \(2010\)](#) studied the effects of sacral acupuncture on acetic acid-induced bladder irritation in rats, focussing on afferent bladder nerve fibres. In the acupuncture group the inter-contraction interval (ICI) of the irritated bladder increased by 35% to near normal values. The ICI also increased in the acupuncture treated, non-irritated bladder, rats. In a third group, capsaicin was used to desensitise the bladder C fibres. Capsaicin, the irritant ingredient of hot peppers, is a neurotoxin that after an initial excitatory response causes afferent nerves to be desensitised or damaged, thereby suppressing painful sensations. Acupuncture did not increase the ICI in capsaicin-pretreated rats, suggesting that sacral acupuncture inhibits abnormal micturition that is mediated via capsaicin-sensitive afferent C fibres. However, this does not reveal the site or mechanism of action of acupuncture other than it being spinal and/or supraspinal.

SNM has revealed fascinating findings on PET scans ([Blok et al., 2006](#)). There is a suggestion that areas of the brain concerned with emotions are gradually reorganised with long-term sacral stimulation i.e. neuroplastic changes occur that may represent a learned reaction to successful therapy. These changes only occur in the 60% of patients for which the treatment is successful. The changes occur in different parts of the brain to those that seem to be affected in the acute phase of neuromodulation. Similar changes may occur with repeat and successful acupuncture treatment.

Acupuncture has been shown using fMRI to have an effect in the limbic system ([Hui et al., 2000](#); [Napadow, 2005](#)). It is thought that decreased neural activity in this area, due to an acupuncture effect, could modulate the experience of pain. These studies have revealed that acupuncture has an effect in structures including the insula, ACC, the PAG and the hippocampus. These are the areas that are increasingly believed to be of importance in bladder function.

However, we are still a long way from understanding where in the neural circuitry acupuncture is actually working. All we can say is that we stimulate a particular segment of the body and generate afferent impulses. This change of activity in one neural pathway modulates a pre-existing abnormal activity through synaptic interactions that results, generally, in a pleasing result for the patient.

## Concluding comments

There is now sufficient clinical evidence and neurophysiological research to justify the confident use of acupuncture in chronic urogenital disease. In clinical practice enhanced mood, sleep and relaxation are observed in most patients, and this can have a profound effect on morbidity.

It seems that the prevailing therapeutic effect is central and probably at limbic system or PFC. General points such as LR3, GV20 and *Shishencong* can be used for their anxiolytic and relaxing effects.

Acupuncture can help in the management of patients with OAB, BPS/IC and CPPS solely or in conjunction with other treatments. These patients are often prisoners of their condition both physically and mentally. In addition they may have longstanding psychological issues. During treatment the acupuncturist should offer the patient maximum encouragement and hope regarding the therapeutic outcome. Recent neurophysiological evidence gives credibility to this approach, in that the PFC and limbic system are almost certainly involved in bladder dysfunction. Evidence from good studies in bladder dysfunction suggests 10–12 sessions of electroacupuncture as effective. The challenge as always is to convince other clinicians and the purchasers of health-care that acupuncture is a viable and conventional adjunctive therapy. Current evidence is pointing in the right direction.

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# Acupuncture for respiratory conditions

A. White

## CHAPTER OUTLINE

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## Introduction

Dyspnoea is physically disabling and can be frightening. The main respiratory causes of dyspnoea are asthma (airways obstruction reversible), chronic obstructive pulmonary disease or COPD (irreversible) and cancer-related dyspnoea. This chapter covers asthma and COPD; cancer-related dyspnoea is covered in the [Chapter 34](#), Acupuncture in Cancer and Palliative Care.

Patients with either asthma or COPD often require long-term medication and may experience acute exacerbations, possibly with repeated emergency hospital admissions which bring additional distress to the patient and costs to society. It is increasingly recognised that important targets of treatment are not only to relieve dyspnoea, but also to prevent exacerbations. Treatment involves a considerable degree of self-management as well as medication. Patients who wish to reduce their dependence on medication may seek acupuncture. While the later evidence suggests that acupuncture may have some role in management, international guidelines specifically warn about the inappropriateness of complementary therapies if they reduce the proper emphasis on education on lifestyle change and life-saving medication.

## Asthma

Asthma is described as: 'A heterogeneous disease, usually characterised by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation' ([www.ginasthma.org](http://www.ginasthma.org) accessed Jun. 2014). Asthma affects at least 300 million people in the world and is an increasing burden on patients, health services and governments,

recognised by the setting up of the Global Initiative in Asthma (GINA) in 1989. Diagnostic criteria for reversible airflow limitation are now standardised.

Asthma is clinically heterogeneous, and many phenotypes have been identified, though these do not necessarily correlate directly with clinical patterns or response to treatment. Categories include allergic asthma, nonallergic asthma, late-onset asthma, asthma with fixed airflow limitation and asthma with obesity (GINA Global Strategy, [www.ginasthma.org](http://www.ginasthma.org)).

GINA guidelines identify the goal of management as prevention of exacerbations and describe in detail a five-step approach (GINA Global Strategy, [www.ginasthma.org](http://www.ginasthma.org)). Avoidance of triggers, modification of lifestyle and medication including preventers and relievers are the mainstay of management. Asthma is in most cases fully controllable, yet it accounts for 1:250 deaths globally, most of which are preventable.

The fundamental pathology of asthma is considered to be bronchial hyperreactivity of immune origin. A variety of stimuli can trigger bronchoconstriction leading to mucus secretion, and an inflammatory response follows.

## EVIDENCE

Underlying challenges for research into acupuncture for asthma include the fact that the placebo effect in patients with asthma can be very powerful, exceeding 10% in 15% of clinical trials included in one review (Joyce et al., 2000). Additionally, there is often a discrepancy between the subjective perception of breathlessness and objective measurements of airflow limitation, especially in the elderly. This emphasises the need to measure both subjective symptoms and objective lung function in research. It also stresses the need not to rely on patients' symptoms but to use objective assessment in the management of asthma.

### Clinical effect in adults

The findings of the current Cochrane Review will be summarised, followed by comments on individual studies.

The Cochrane Review is based on 12 studies available in 2004 (McCarney et al., 2004), and no new studies were found in updated searches in 2008. The trials were mostly small, Table 28.1. Outcomes included forced expiratory volume in 1 second (FEV1), peak expiratory flow rate (PEF) and quality of life (QoL). Because of disparity between the studies in design, outcomes and intervention, data from only two small studies could be included in a meta-analysis. This showed no difference in FEV1 (standardised mean difference, SMD 0.12; 95% CI -0.31, 0.55) and no difference in QoL. Two other trials showed reduction of medication use in the acupuncture group; four studies measured symptoms, which showed no meaningful differences. The overall problem in drawing conclusions is the lack of power. The authors included the following in their conclusion: 'Some studies did report significant positive changes in subjective parameters, and medication use, which suggest that some patients with asthma may benefit from acupuncture'.

The largest trial in the Cochrane Review randomised 66 patients with mean age about 40 years, and a 10-year history of mild-moderate asthma, into three groups (Medici et al., 2002). The acupuncture group ( $n=23$ ) were treated with a standardised acupuncture formula with 11 points in total (Table 28.2); the 'sham' control group ( $n=23$ ) had exactly the same treatment given at 11 non-acupuncture points close to real acupuncture points. Twenty patients had usual care alone. The main outcome was PEF variability, at 10 months, which showed no difference between the three groups. In WMA terms, the supposedly sham intervention was likely to be active, though neither acupuncture group showed clinically important differences compared with usual care.

TABLE 28.1 ■ Study data extracted from Cochrane Review (treatments described in Table 28.2)

References	N (analysed) design	Outcome	Limitations
Biernacki and Peake (1998)	23 (22) Crossover DB	QoL improved, rescue medication reduced: no difference between groups	Sham may have been active
Christensen et al. (1984)	18 (17) Parallel DB	PEF, symptoms, drug use: all results seem to favour acupuncture	Real group more severe than sham at baseline
Dias et al. (1982)	20 Parallel DB	PEF, symptoms, drug use: all results seem to favour sham acupuncture	Heterogeneous sample. Breathing exercises not standardised. Inconsistent number of sessions. Sham may have been active
Hirsch and Leupold (1994)	39 (32) children Crossover DB	No significant differences in peak flow, symptoms or drug use	Incomplete reporting
Joos et al. (2000)	38 Parallel PB	No changes in lung function. Subjective improvement 15/20 real, 8/18 controls (NSD). Drug use significantly reduced after real acupuncture	
Malmstrom et al. (2002)	27 Parallel (Induced attack) PB	No difference between groups in PEF, drug use	
Medici et al. (2002)	66 Three parallel groups Partial DB	Acupuncture significantly better for PEF variability; number of attacks, drug use and QoL no difference	Sham may have been active
Mitchell and Wells (1989)	31 (29) Parallel DB	No significant differences	Sham may have been active
Najafizadeh et al. (2006)	26 Parallel	FEV drugs symptoms: effect not reported	Conference abstract
Shapira et al. (2002)	23 Crossover DB	No significant change in lung function, bronchial reactivity or symptoms	Some missing data Sham may have been active
Tandon et al. (1991)	15 Crossover DB	No significant effects within or between groups (PEF and FEV1)	
Tashkin et al. (1985)	25 Crossover DB	No significant differences between or within groups	

DB, double blinded (patients and evaluators); NSD, no significant difference; PB, patient blinded; PEF, peak expiratory flow rate; FEV1, forced expiratory volume in 1 second.

TABLE 28.2 ■ Interventions for asthma: data extracted from Cochrane Review

References	Points used <sup>a</sup>	Control(s)	Regime
Biernacki and Peake (1998)	CV17	Nonpoint on chest wall	One session
Christensen et al. (1984)	LI4, <i>Dingchuan</i> , BL13, CV17 EA 4/100Hz	Three nonpoints (hand and scapula) superficial, sham EA	Ten sessions in 5 weeks
Dias et al. (1982)	CV22, <i>Dingchuan</i> , LU7 (unilateral)	GB5, GB6	Two to eight sessions
Hirsch and Leopold (1994)	(Laser) <i>Dingchuan</i> , LU1, LU5, LU7, LI4, CV17, BL13, BL17, KI3, SP6	Sham laser, same points	Fifteen sessions, twice weekly
Joos et al. (2000)	BL13, CV17, LI4, LU 7 and up to four additional flexible points bilateral based on TCM diagnosis (e.g. LU5, LU6, ST36, ST40, KI3, KI7, SP6, SP9, CV6, CV12, HT7)	GB8, GB34, TE3, TE7 and up to four additional points not used for asthma	Twelve sessions in 45 weeks
Malmstrom et al. (2002)	Individualised (5 needles increasing to 16) from LU5, LU6, LU7, PC6, CV17, BL13, GV20, ST36, ST40, KI3	Sham TENS on upper chest	Twenty sessions in 15 weeks
Medici et al. (2002)	'Antiasthmatic' GV14, <i>Dingchuan</i> , BL13, KI3, LU10, SP6 'Anti-inflammatory' LI4, LI11, GV14, ST36 'Antiallergic' ST36, LR13, PC6	(1) Ten millimetre depth at nonpoints close to real points (2) No treatment	Sixteen sessions, in two series of 8 over 4 weeks with 8-week gap
Mitchell and Wells (1989)	BL13, CV17, EX17(?), LR3	SP8, KI9, GB37 with same depth, manipulation, <i>de qi</i>	Eight sessions in 12 weeks
Najafizadeh et al. (2006)	EA, no further details	Sham EA, no further details	Ten sessions in 4 weeks
Shapira et al. (2002)	TCM approach, no details	Sham: subcutaneous insertion, nonpoints back, shoulders, extremities	Four sessions in 2 weeks
Tandon et al. (1991)	(Laser): eight body points (SP6, ST36, LR9, LI11, CV17, CV22, BL13, <i>Dingchuan</i> ) and three ear points (asthma, lung, internal secretions)	Sham laser at sham points: GB34, LR8, LR14, SI3, SI6, BL18, BL25 and two ear points (uterus and bladder)	Ten sessions in 5 weeks
Tashkin et al. (1985)	LI4, GV14, ST36, LU7, <i>Dingchuan</i> , ExWaitingchuan (?)	Sham at nonpoints (?location)	Eight sessions in 4 weeks

<sup>a</sup>Bilateral needling with manual stimulation unless stated (?) location cannot be verified.

In a subsequent RCT, Choi and colleagues randomised 45 patients to 12 sessions of acupuncture, sham acupuncture or waiting list, all continuing usual medications (Choi et al., 2010). There were no significant differences between the groups for weekly average PEF or FEV1. However, both QoL and symptoms (reported as transition dyspnoea index) were significantly improved in the real acupuncture group compared with usual care controls.

Some other sham-controlled studies have shown improvements in symptoms, wellbeing or QoL after acupuncture (Dias et al., 1982; Joos et al., 2000) without changes in objective dyspnoea measurements. And improvements in QoL appear when acupuncture is compared with no acupuncture.

It is relevant to comment that some studies do not seem to have given acupuncture ‘a fair chance’, whether because of probably inadequate acupuncture technique, or active control, or small sample size, or because asthma was already under optimal control. For example, Shapira et al. (2002) gave four sessions of individualised TCM acupuncture to 23 adults followed by sham acupuncture (subcutaneous needling at non-sites, with manual stimulation) after a 3-week washout period. In view of the small number of sessions, it is not surprising that no changes were seen in any of the outcomes measured.

Most studies in the Cochrane Review are controlled by sham acupuncture with needle insertion into the so-called ‘irrelevant’ points, often with manual stimulation – which could be active. One exception is Malmstrom et al. (2002) ( $n=27$ ) where the control was sham TENS to the upper chest. After 20 sessions of one or other, there was no difference between groups in bronchial responsiveness to an induced asthma attack.

A review and meta-analysis of studies in which real and sham points were compared included data from 9 of 11 possible RCTs (Martin et al., 2002). These reviewers analysed SMDs, allowing more studies to be combined than in the Cochrane Review which used mean differences. The outcomes were peak expiratory flow rate (PEFR), FEV1 or forced vital capacity (FVC), but a single outcome was chosen for each study, and the estimated SMD converted to FEV1. The authors sought individual patient data, but these were available for only three studies.

As Table 28.3 shows, there was no evidence of a significant effect of acupuncture overall. However, all the four studies that tested the effect of reversing experimentally induced bronchoconstriction (by exercise in three, by methacholine in one) showed a significant effect. This is discussed with other evidence in the later section. The reviewers (Martin et al., 2002) comment that these findings are limited by lack of overall sample size, missing information and use of possibly active points in the control groups.

TABLE 28.3 ■ Pooled estimates (SMD) from meta-analysis of results of sham-controlled trials expressed as FEV1 (Martin et al., 2002)

Study design	Improvement in FEV1 (SMD)
All studies (9)	1.7 (95% CI -1.3, 4.7)
Bronchoconstriction induced (4)	0.3 (95% CI 0.04, 0.56)
Bronchoconstriction not induced (5)	-0.08 (95% CI -0.28, -0.20)

### Cost-effectiveness

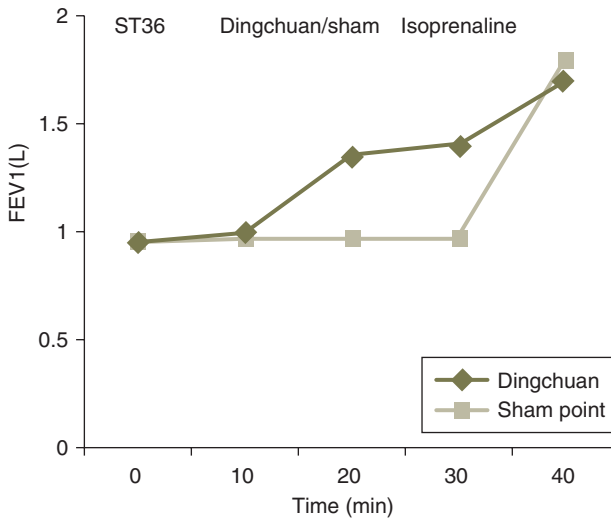
The cost-effectiveness of acupuncture for asthma was tested in an RCT in Germany in which 306 patients were randomised to either immediate acupuncture or a 3-month wait before acupuncture (Reinhold et al., 2014). The QoL in the acupuncture group was 9% higher than in the control group at 3 months and, interestingly, continued to increase subsequently. Only health-care utilisation costs were measured, and acupuncture proved cost-effective (ICER between €23,231

and €25,315, inside the €50,000 threshold quoted). The authors comment that, because of reduction in acupuncture costs since the time of the study, and because of the short study period, this calculation is likely to underestimate acupuncture's cost-effectiveness.

### Acute effect on bronchoconstriction

A number of early studies tested an acute effect of acupuncture either during an attack of asthma, or after challenge with a trigger, usually methacholine or histamine.

In one (Yu and Lee, 1976) 20 patients with acute bronchoconstriction were given acupuncture at ST36 of the right leg (as an initial control) followed by acupuncture at either *Dingchuan* (0.5 cun either side of the spinous process of C7) or a site 4 cm lateral to *Dingchuan* – bilateral in both cases. Finally, inhaled isoprenaline was given to achieve full bronchodilation. As shown (Fig. 28.1) there was a significant rise in mean FEV1 after acupuncture at *Dingchuan* (but not ST36 or the sham points) and after isoprenaline inhaler.



**Figure 28.1** Changes to FEV1 during successive interventions: acupuncture at ST36, acupuncture at Dingchuan or sham and isoprenaline inhaler.

Takishima et al. (1982) gave acupuncture to 10 patients with asthma while in a controlled breathing chamber that allowed measurement of bronchial resistance. Acupuncture was given insertion at a neck point (*Suitotsu*, a point dangerously close to the internal carotid artery) with manual stimulation, and sham acupuncture was to the next higher vertebral level without stimulation. Experimental sessions were repeated. One of 17 sham treatments produced a 20% response, compared with 16/26 real acupuncture treatments.

Tandon and Soh (1989) compared real acupuncture at *Dingchuan*, CV17, LU6, LU7 with sham acupuncture at TE5, ST25 and GB34 in 17 patients with moderately severe asthma. Needles in both groups were stimulated every 5 min for 20 min. The study was patient and observer blind. There was no significant change in bronchoconstriction response to histamine in either group and no difference between groups. This suggests that any effect is not point specific.

In a crossover study ( $n=16$ ), the effect on FEV1 of real acupuncture (LU7, LI4, PC6, ST40, LI11 and PC3 with manual stimulation) was compared with sham acupuncture (two nonpoints on the extremities with superficial insertion and no stimulation) (Chu et al., 2007). Real acupuncture showed a 12% increase in FEV1 compared with 0.3% after sham.

## Clinical points

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Moderate evidence suggests acupuncture has an acute effect on induced bronchoconstriction.

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Fung et al. (1986) conducted a crossover study in 19 children with exercise-induced asthma to compare real acupuncture (LU6, KI3 and *Dingchuan*), sham acupuncture (LI4, PC4 and GB39, with the same stimulation) and no acupuncture. All measures of airflow after exercise were beneficially affected by acupuncture; for example, FEV1 increased 44%, 33% and 24% in the three groups, respectively.

The pooled evidence from Fung et al. (1986) and three other sham-controlled studies in induced asthma (Chow et al., 1983; Morton et al., 1993; Tashkin et al., 1977) is presented earlier, in Table 28.3.

## Asthma in children

In children and adolescents with asthma, two RCTs have shown promise. Scheewe and colleagues randomised 93 adolescents, aged 12–17 years, who were undergoing rehabilitation training in the form of behaviour therapy, asthma sports and climate therapy (Scheewe et al., 2011). Forty-six children received 12 sessions of acupuncture over 4 weeks (using points BL13, CV17, LU7 plus two optional points depending on TCM diagnosis). The control group had physician-led discussions. Both groups improved over the 4 weeks, but the acupuncture group improved more in terms of PEF and anxiety, but not in lung function or QoL.

Another study in 122 much younger children (6 months to 6 years) also compared 3 months' acupuncture with no acupuncture (Karlson and Bennicke, 2013). Asthma diaries were kept for 3 and 12 months. Symptom scores and use of inhaled steroids were significantly reduced in the acupuncture group at 3 months, though the effect was not seen at 12 months.

## TENS

In a study on 20 patients by Sovijärvi and Poppius (1977), the effect of a sequence of adaptation, dummy TENS, active TENS (50 Hz) and isoprenaline was studied by measuring PEF. Eleven patients' PEF increased significantly following placebo TENS and then did not improve further when true TENS was added. All patients showed an increase in PEF after isoprenaline. The authors concluded that the bronchodilator effect of TENS was psychogenic. However, they did not discuss the possibility that the mode of active stimulation may not have been optimal and if an inappropriate active mode was used one could not have expected further improvement. If all modes of stimulation were to be tested, then conclusions would be interesting.

An RCT on acupuncture-like TENS in 43 children showed no effect on lung function (Lin et al., 2010). However, a response in exercise-induced asthma was shown in an RCT (Ngai et al., 2009): TENS over *Dingchuan* and LU7 for 45 min before exercise reduced the decline in FEV1 after exercise: a third group with TENS both before and during exercise showed an even greater improvement in FEV1.

## LASER THERAPY

Tandon et al. (1991) carried out a double-blind, placebo-controlled crossover study in patients with chronic asthma using points SP6, ST36, LU9, LI11, CV17, CV22 and BL13 plus ear points as active, and GB34, LR8, LR14, SI3, SI6, BL18 and BL25 as placebo points, with a washout period in between. They failed to show any significant difference between therapies in subjective and objective testing or in the need for additional medication.

Morton et al. (1993) gave 13 subjects laser therapy, placebo laser, salbutamol or no treatment in random order prior to an exercise test. The treatment was given to points CV17, BL13, GV14,

LU7 and KI3, at 1.5 mW for 20 s and patients were blinded to laser or placebo therapy. The authors concluded that the laser treatment showed no difference from placebo in all measures. However, they did not vary the mode of stimulus and therefore it remains to be tested whether different modes of stimulation would give the same results.

A review of sham-controlled studies of laser acupuncture in children found three RCTs in 176 patients: one parallel group study was positive, two crossover studies were negative (Zhang et al., 2012). The authors concluded: ‘No compelling evidence exists to suggest that laser acupuncture is not an effective treatment for childhood asthma’ and recommended further studies.

## MECHANISMS

Various studies have suggested a mode of action for acupuncture, on either bronchoconstriction or inflammation. In a rat model of asthma, seven sessions over 2 weeks of EA to GV14, BL13, *Dingchuan*, LU1, CV17 ST36 and SP6, at sufficient intensity to cause muscle contraction, reduced peribronchial and perivascular inflammatory cell infiltrates in bronchial lavage and pulmonary tissue, compared with sham acupuncture (similar stimulation to nonpoints) and no acupuncture controls (Carneiro et al., 2005). The same research group subsequently showed that acupuncture decreased the release of cytokines (including LTB4 and NO) in correlation with the reduction in eosinophils infiltration (Carneiro et al., 2010).

Joos et al. (2000) compared a course of 12 sessions of acupuncture over 4 weeks with sham acupuncture with superficial needle insertion into ‘inappropriate’ points in the limbs (specifically avoiding the trunk: TE3, TE19, GB8, GB34, and random selection from BL38, BL55, ST4, ST6, ST32, TE14, TE23, SI5) in 38 randomised patients with asthma. There were significant improvements in wellbeing in the acupuncture group, accompanied by increases in the population of lymphocytes and lymphocyte proliferation; and changes in cytokines indicating reduced inflammatory response, that is, increase in IL8, and reductions in IL6 and IL10. The eosinophils count was reduced. The authors suggest the mode of action might be through autonomic modulation of the immune system.

These findings were supported in an (uncontrolled) study in humans by a Chinese research group (Yang et al., 2013), who found an immunomodulatory effect on inflammatory cells and cytokines. The same group (Xu et al., 2012) then studied the effector proteins specific to acupuncture at GV14, BL12 and BL13, using proteomics methods in an animal model, and were able to identify individual proteins from the inflammation regulation pathway that were either up- or downregulated by acupuncture (Li et al., 2012).

## CLINICAL APPROACH

In a seminal paper, Cheng (2009) considered the physiological basis of points that were recommended in classical acupuncture texts for various conditions. For asthma, the common point in all traditional prescriptions was BL13, known as the *Shu* point for the lungs, which Cheng notes corresponds to the sympathetic ganglion at the level of T3.

Other points Cheng extracted from five traditional texts are mostly located in areas that are segmentally related to the lungs; the lower neck and upper back, *Dingchuan* (0.5 cun either side of the spinous process of C7) and BL points, TE17, GV14; the sternum (CV17 and CV22); and the forearms (PC6, LU5, LU6, LU9, LU10 and LI4). One text recommends a point on the leg, ST40. Practitioners are reminded that a good knowledge of the anatomy of the pleura is needed because of the high risk of pneumothorax from needling over the thorax.

Table 28.2 gives the points used for asthma in clinical trials included in the Cochrane Review.

In summary, while evidence does not suggest acupuncture as a regular treatment for chronic asthma, acupuncture may well be worth adding to standard asthma care in the hope of improving

QoL and avoiding repeated exacerbations leading to hospital admission. There is little published on the clinical use of asthma in acute bronchospasm, though research suggests this could be further explored. It should be remembered that acupuncture may reduce subjective symptoms without improving airflow, and so objective assessments are vital to the correct management of asthma.

## Chronic obstructive pulmonary disease

COPD is an umbrella term for a number of conditions that cause limitation of pulmonary air flow, with symptoms of dyspnoea, excessive sputum production and chronic cough (<http://www.who.int/respiratory/copd/en/> accessed Jun. 2014). It is the subject of the Global Initiative for Obstructive Lung Disease, who set criteria for diagnosis using spirometry ([www.goldcopd.org](http://www.goldcopd.org) accessed Jun. 2014). The main risk factors for COPD are tobacco smoking, air pollution both indoors and outdoors, and occupational dusts and chemicals. It affects 64 million people worldwide and is slowly progressive involving gradual loss of lung function. It caused an estimated 3 million deaths globally in 2005, 5% of all deaths. Deaths are projected to further increase by 30% by 2023 because of the increase in smoking. Symptom management involves reduction of avoidable risk factors, use of bronchodilators and physical therapy. Continuous oxygen therapy is appropriate for some patients and may prolong life – the only intervention that may alter the course of the condition.

## EVIDENCE

In a classic early RCT on acupuncture for COPD, Jobst and colleagues selected 26 patients, all meeting the criteria for COPD, but four also having features of reversible airways obstruction (Jobst et al., 1986). Patients were randomised to acupuncture using individualised TCM, or a sham treatment with needles over the patella: patients were placed in clinically matched pairs so that the person in the sham group had the same number of needles and use of moxibustion as the partner. All participants were under the impression they were receiving active treatment. Thirteen treatments were given over 3 weeks. Eight different assessments were used at baseline and end of treatment. The acupuncture group showed significantly greater improvement in all subjective scores and the distance walked in 6 min – which increased by over a third. General wellbeing increased in the acupuncture group by 51% and in the sham group by 39%, a significant difference. Neither PEF nor other spirometric indices changes significantly in either group.

Two feasibility studies demonstrated the practicality of providing acupuncture for COPD in hospital and domiciliary environments, respectively, though finding recruitment slow. Neither was designed to show treatment effects, so results are not reported. In a crossover study ( $n = 16$ , of whom 12 completed), Davis et al. (2001) compared acupuncture (needles left for 20 min followed by semipermanent studs), sham studs with cut-off points, and sham TENS for 20 min. All treatments were given at the patient's home, to CV20, CV21 and LI4, a formula previously recommended for disabling cancer-related breathlessness (Filshie et al., 1996). In another study ( $n = 11$ ), Whale and colleagues compared acupuncture and the Park sham device in patients admitted to hospital for exacerbation of COPD (Whale et al., 2009).

Neumeister et al. (1999) compared seven acupuncture or placebo acupuncture sessions over 2 weeks in patients with stable COPD ( $n = 10$ ). Effects were assessed by pulmonary function tests as well as the chronic respiratory disease questionnaire. The acupuncture group improved significantly in FEV1 and QoL, but the placebo group reported only a slight improvement of QoL and a deterioration of lung function.

In an RCT that analysed results on 41 patients (out of 70 enrolled), QoL improved 19-fold after acupuncture, sevenfold after acupressure (Maa et al., 2003) though there was no significant difference in objective measures of breathlessness. The paper was titled as 'chronic asthma', but diagnosis is unclear. Points used were LU1, PC6, Dingchuan, GV14 and ST36.

Suzuki and colleagues conducted three studies of increasing rigour culminating in a blinded RCT. A case series ( $n=26$ ) of weekly acupuncture showed significant improvement in the several outcomes including the Borg dyspnoea scale after 10 weeks of acupuncture treatment from 4.02 (2.85) to 1.96 (1.97) (Suzuki et al., 2012). They then compared adjunctive acupuncture with standard medication alone using a matched pairs design ( $n=30$ ), showing a significant reduction in the Borg scale at 10 weeks ( $2.2 \pm 2.7$  vs.  $6.4 \pm 3.4$ ,  $p=0.0001$ ), as well as improvements in 6-min walking distance and oxygen saturation (Suzuki et al., 2008).

They randomised 68 patients with COPD (stages II to IV) to 12 weekly sessions of acupuncture at LU1, LU9, LI18, CV4, CV12, ST36, KI3, GB12, BL13, BL29 and BL23 (Suzuki et al., 2012). The sham control group had Park sham needles applied to the same points. At the end of treatment, the primary outcome, modified Borg scale after the 6-min walking test, improved from 5.5 (2.8) to 1.9 (1.5) in the acupuncture group. In the sham group, it changed from 4.2 (2.7) to 4.6 (2.8). The difference was statistically significant and clinically important. Acupuncture was also superior for walking distance, oxygen saturation and QoL score, though not for FEV1. There was no long-term follow-up.

### Acupuncture as adjunct to rehabilitation

Deering et al. (2011) conducted a three-arm study ( $n=60$ ) of acupuncture as an adjunct to intensive pulmonary rehabilitation (PR) for severe COPD – twice weekly exercise and education over 2h, inspiratory muscle training and unsupervised home exercises. Nineteen controls were on a waiting list for 8 weeks. Twenty-five had PR alone, 16 had PR and acupuncture, consisting of seven weekly sessions using points LI11, LI10, TE10, TE6, LU5 and LU7. Stimulation details are not reported. The primary outcome measure was a change in measures of systemic inflammation (interleukins, TNF alpha and C-reactive protein), and various symptom and lung function tests were secondary. There were no changes in any group in measures of inflammation. Both groups receiving PR had significantly improved QoL scores, reduced dyspnoea scores, improved exercise capacity and maximum inspiratory pressure, compared with the untreated controls. The only benefit of additional acupuncture identified in this study was reduction of breathlessness at rest. However, the sample size was small, and there may have been a ‘ceiling’ effect of the intensive exercise making further improvement impossible.

A systematic review of the Chinese literature, including 32 RCTs of overall poor quality, is somewhat difficult to interpret (Li et al., 2012). The authors found acupuncture combined with Western medicine increased FEV1 more than Western medicine alone (five studies), but there was no difference when they were directly compared (three studies). There were no differences between acupuncture and traditional Chinese medication.

### ACUPRESSURE

In a crossover study ( $n=31$ ) patients beginning a 12-week rehabilitation programme were randomly assigned self-acupressure at real or sham points for 6 weeks, in random order (Maa et al., 1997). Real acupressure was more effective than sham acupressure for reducing dyspnoea, but sham acupressure seemed more effective for reducing peripheral sensory symptoms.

The group's subsequent RCT (described earlier) reported a sevenfold increase in QoL but no change in objective evaluations after self-acupressure for 8 weeks (Maa et al., 2003).

Patients diagnosed with COPD ( $n=44$ ) were randomised to acupressure at either true or sham points (Wu et al., 2004). Five sessions were given weekly, for 4 weeks. True acupressure was given at GV14, CV22, BL13, BL23 and LU10. Sham acupressure used SP5, SP6, SP3 and LR1, specifically chosen not to stimulate relevant spinal segments. The protocol was unusually rigorous to reduce performance bias. The pulmonary function and dyspnoea scores, 6-min walking distance measurements, state anxiety scale scores and physiological indicators of the true acupuncture point acupressure group improved significantly compared with those of the sham group.

The study was replicated in elderly patients ( $n=44$ ) with COPD, mean age 74 years (Wu et al., 2007). They found the same significant effect on dyspnoea scores and oxygen saturation after 4 weeks' treatment compared with sham and also found the Geriatric Depression Scale scores were significantly improved after real acupressure.

Another group from Taiwan conducted an RCT of patients with COPD receiving mechanical ventilation assistance over 21 days (Tsay et al., 2005). Acupressure was given to PC6 and LI4 together with *Shenmen* in both ears, daily for 10 days. This group also had massage, and the control group had massage and handholding. Dyspnoea, anxiety and physiological indicators improved significantly more in the acupressure group than the controls.

These results suggest that acupressure therapy improves dyspnoea in terms of perceived symptoms, QoL and (less convincingly) objective measures, as well as reducing the associated psychological problems.

## TENS

Two studies tested for an acute effect: 46 outpatients with an average age of 75 years received a 45-min session of either TENS (4 Hz, pulse width 200  $\mu$ s) or sham TENS over the point *Dingchuan* (0.5 cun lateral to C7 spinous process, bilaterally) (Lau and Jones, 2008). The TENS was delivered to the 'point' only by shielding the surrounding area of skin with plastic film. The increase in FEV1 after TENS was 0.12 L (95% CI 0.07–0.15) greater than after sham TENS. The increase was about 10%, just short of clinical significance. The FVC showed a nonsignificant trend in the same direction.

Another RCT ( $n=44$ ) found a 24% greater increase in FEV1 with TENS than with sham TENS, as well as significant increases in dyspnoea VAS and in respiratory rate (Ngai et al., 2013). There was an 18% greater increase in serum beta-endorphin levels after TENS, which correlated with the increase in respiratory rate.

A three-arm RCT ( $n=28$ ) compared TENS or sham TENS at *Dingchuan*, with the third arm given sham TENS over the patella (Ngai et al., 2010), all 5 days a week for 4 weeks. In the TENS group, FEV1 increased significantly by  $8.2 \pm 2.4\%$ , which was significantly better ( $p=0.008$ ) than the increase of  $1.1 \pm 2.6\%$  from sham TENS at *Dingchuan*, and the decrease of  $5.4 \pm 3.5\%$  in the TENS to the patella. The increase in 6-min walking distance was also significantly greater in the acupuncture group; other evaluations of respiratory function showed mostly nonsignificant trends, but all in favour of TENS.

## MECHANISMS

Little is known about possible mechanisms by which acupuncture, acupressure and TENS might influence COPD.

Suzuki et al. (2012) suggested the mechanisms of reduction of overwork fatigue of the accessory muscles of respiration, also improving mobility of the rib cage. They also suggested that a reduction of breathlessness at mealtimes led to improved nutrition.

Using an animal model, Geng et al. (2013) showed that EA to ST36 given during the induction of the lung changes by cigarette smoke had several favourable effects: lung resistance was decreased, as was bronchial and bronchiolar obstruction; lung compliance increased; and levels of TNF- $\alpha$ , IL-1 $\beta$  and MDA in the bronchioalveolar lavage fluid were reduced, though not to baseline values. This suggests that acupuncture may downregulate inflammatory cytokines.

## Concluding comments

As with acupuncture in many internal diseases, much of the data on acupuncture for asthma remain conflicting. It probably has a short-term effect on acute bronchoconstriction, and a number of reports suggest it may lead to improvements in QoL. In COPD, two RCTs of acupuncture

reached conflicting results, but studies on acupressure and TENS repeatedly report both objective and subjective improvements. The accessibility of the respiratory system for objective testing and the established questionnaires for subjective evaluation afford the opportunity for further study so that firm conclusions can be made.

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# Acupuncture for ear, nose and throat conditions

A. White

## CHAPTER OUTLINE

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## Introduction

In 1974 Felix Mann reviewed his clinical experience of acupuncture and ENT conditions (Mann, 1974). He thought that acupuncture was of definite benefit in motion sickness, and of moderate benefit in rhinitis, recurrent tonsillitis and some cases of vertigo; it was useful in a small percentage of patients with tinnitus but had nothing to offer for deafness. That review was remarkably perceptive, and these clinical impressions have been largely supported by the (rather limited) research that has been performed since then.

ENT-related topics that are dealt with in other chapters include temporomandibular pain (Chapter 38), trigeminal neuralgia (Chapter 38 and 19) and xerostomia (Chapter 34).

## Deafness

It should be self-evident that acupuncture cannot hope to affect a structural problem such as sensorineural deafness. However, a US physician paid an early visit to China in 1971 and reported that acupuncture had recently been introduced there as 'treatment' for deaf children (Rosen, 1974). Some Western doctors were seduced by the enthusiastic confidence of the Chinese doctors and the supposed 'magical' benefit of this simple therapy for a distressing condition. But it seems that acupuncture may have been over-promoted as an example of Communist achievements, and no proper evaluation was carried out. Uncritical reports soon circulated in the American press that acupuncture was being used for deafness. As a result, many patients with deafness self-funded acupuncture treatment in the desperate hope of cure and were deeply disappointed by the lack of improvement. So, just as interest in acupuncture was growing, its reputation was greatly undermined by these failures (Hussey, 1974).

Carefully conducted trials, for example by [Madell \(1975\)](#) and [Yarnell et al. \(1976\)](#), soon confirmed that acupuncture had no effect on sensorineural deafness. Any small subjective changes that some patients had reported were probably the result of desperate hope; minor variations in audiometric measurements that had been reported were due to either natural variation or the lack of skill among technicians ([Liu et al., 1982](#)).

### Clinical points

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Acupuncture should not be expected to affect sensorineural deafness.

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The only recent literature on this subject is from Asian authors and concentrates on acupuncture in patients with sudden sensorineural hearing loss. One case associated with dizziness was reported ([Huang and Li, 2012](#)), but natural remission occurs in this condition, so isolated case reports can be misleading.

A possible mechanism of neuroprotection of hair cells is discussed in the next section.

## Tinnitus

Tinnitus affects about 10% of the population, 1–3% of them severely ([Langguth et al., 2007](#)). Tinnitus has many causes ([Ciuman, 2013](#)) and exists in many forms – such as in association with hearing loss, hyperacusis, phonophobia, Meniere's syndrome or drug side-effects – and may be heard unilaterally, bilaterally or centrally in the head. It is best regarded as a result of neuroplasticity, and its comparability with chronic pain suggests that acupuncture might be a valuable therapy for some forms of the condition. In addition, [Travell and Simons \(1983\)](#) described unilateral tinnitus associated with myofascial trigger points in masseter muscle, without any impairment of hearing.

No studies have specifically explored which types of tinnitus respond and which do not, and no studies have explored the mechanisms of acupuncture or the appropriate treatment regime. Unsurprisingly, then, the evidence overall suggests little effect at the group level.

A systematic review of sham-controlled RCTs included only nine ([Kim et al., 2012a](#)). Several studies used treatments with clearly inadequate numbers of points or treatment sessions. The most common local points used were GB2, GB20, GB12, TE17, TE21, TE22, SI9 and GV20, together with various limb points and sometimes other GV points. Five sham-controlled studies showed no overall effect, although two RCTs using a single session of scalp acupuncture showed positive effects.

Only two studies were of minimum risk of bias, one of which was published in English ([Jeon et al., 2012](#)). In that study, 33 participants received 10 sessions of acupuncture or sham with needles in local non-points; only 14 were available for assessment at 3-month follow-up. There was evidence of an effect on tinnitus Visual Analogue Scale (VAS) but not when assessed with three other questionnaires. Given the small sample and the possibly active sham, the trend shown in this study justifies further studies.

Several studies used other designs. An RCT by [Furugard et al.](#) was excluded from this review as it was not sham-controlled. Twenty-two participants with disabling tinnitus received either manual acupuncture or individualised physiotherapy ([Furugård et al., 1998](#)). The VAS scores for loudness, annoyance and awareness of tinnitus together with the Nottingham Health Profile (NHP) were used to evaluate the effects. There was immediate, significant relief in terms of loudness and annoyance after acupuncture and significant improvement in NHP scores. There were no significant changes after physiotherapy. No subjects in either group rated themselves as 'cured'. The percentages of subjects who rated themselves as 'greatly improved' by acupuncture and physiotherapy were 45% and 16%, respectively, while the percentages of subjects who rated themselves as 'improved' were 55% and 84%, respectively. However, annoyance and NHP scores returned to pretreatment levels at 1-year follow-up.

A four-arm study compared manual acupuncture with behaviour therapy and cinnarizine, and sham versions of each (Podoshin et al., 1991). Subjects assessed the degree to which tinnitus interfered with their daily activities on a five-point scale. Behaviour therapy was the most effective intervention; 3 out of 10 of the acupuncture patients showed an improvement.

## POSSIBLE MECHANISM

Acupuncture is used to treat progressive deafness and tinnitus in the East. Seeking possible mechanisms, Maeda and colleagues used an animal model of progressive deafness, p75-knockout mouse (Maeda et al., 2014). 1 Hz EA at SI19 and TE17 twice weekly for 4 months appeared to protect the organ of Corti cells and hair cells from the expected deterioration over time. This points to a possible neuroprotective effect that may be relevant to further studies.

The balance of this evidence is that acupuncture research on tinnitus is still immature, there are promising results in some patients, and preliminary studies are necessary to find the most appropriate form of acupuncture and those patients most likely to respond. Acupuncture may have a supportive role in a therapeutic programme for tinnitus alongside cognitive and relaxation techniques, but it may be necessary to continue therapy in the long term for a sustained effect.

## Vertigo

True vertigo occurs with tinnitus and deafness in disorders of the central or peripheral vestibular mechanism, which are irreversible. But the differential diagnosis of the complaint of vertigo includes cerebral, musculoskeletal and cardiovascular disorders (Ciuman, 2013), some of which may be open to symptom relief.

In a participant-blinded RCT, 204 patients with acute vertigo – mainly identified by tests for vestibular function, but also from other sources – were randomised to acupressure device (Sea-Band) placed either PC6 or the dorsal surface (sham) by a blinded assistant (Alessandrini et al., 2012). Nausea and vomiting were significantly less in the verum group, but vertigo was unaffected.

No RCTs in English are found in the usual databases. In the absence of controlled trials we are left with clinical impressions: Mann (1974) suggested that older patients with mild vertigo may be helped, and this view is supported by Campbell (2001) who suggested that periosteal treatment of the cervical vertebrae may reduce the symptoms in moderate cases.

## Motion sickness

Once it was recognised that acupuncture significantly reduced the nausea and vomiting of pregnancy, chemotherapy and general anaesthesia (Dundee and McMillan, 1991), it was logical to see whether stimulating PC6 had any effect on motion sickness since the symptoms are somewhat similar. Warwick-Evans et al. (1991) conducted a well-designed double-blind trial of acupressure. Matched pairs of healthy volunteer students were treated with either acupressure at PC6 with Sea-Bands, or placebo acupressure with Sea-Bands placed 5 cm proximal to PC6 and deactivated by removing the stud. Vertigo was assessed after the subjects had been rotated in a chair at eight rotations per minute while tilting their heads forwards then backwards every 2 s in a standardised way. The acupressure had no effect on their symptoms and signs of motion sickness, although it should be pointed out that the stimulus could be inadequate, particularly with such a strong motion cue.

In contrast, Hu et al. (1992) studied the effect of surface electrical stimulation across the wrist at PC6 and TE5 through metal plates on flexor and extensor surfaces of one wrist. Motion sickness was induced by sitting the subjects inside a standardised rotating optokinetic drum. Subjects were able to control the intensity of the electrical stimulation themselves. Both the symptoms of motion sickness and measurements of gastric contraction were significantly reduced by electrical stimulation of PC6 when compared with inactive placebo stimulation.

Hu et al. (1995) repeated the above study with 64 undergraduate students who were randomised to four groups: they received either finger pressure on PC6, or finger pressure on a dummy point, or light finger contact without pressure at PC6 (sham), or no intervention. The finger pressure or contact was repeated at 1 min intervals throughout the time the subject sat in an optokinetic drum (24 min). The mean nausea ratings clearly indicate that PC6 acupressure has a statistically significant effect. Simultaneous recordings of gastric activity and tachyarrhythmia support these findings.

In a crossover study, 16 people who reported motion-related sickness and did not respond to placebo in a preliminary test drove a simulator for 15 min wearing acupressure device, an electrical stimulation device or a placebo device (Cox et al., 2011). The acustimulation device, but not acupressure, was effective at reducing physical discomfort.

No other studies were found field-testing acupressure in conditions that generate sea-sickness or other forms of motion sickness. However, a published letter reported dramatic responses to auricular acupuncture (topped up by body acupuncture if necessary) during flights conducted in parabolic arcs to simulate weightlessness during training for space travel (Volf, 2010).

## Meniere's disease

A systematic review of acupuncture for Ménière's syndrome included 9 English and 18 Chinese language studies (Long et al., 2011). Only six were controlled trials, and all but one of the studies were conducted in China, mostly using a graded scoring approach (such as 'cured', 'effective/improved' not effective'). The studies covered body acupuncture, ear acupuncture, scalp acupuncture, fluid acupuncture point injection and moxibustion. The studies were of varying quality. Two of the three RCTs using fixed point treatments with acupuncture were positive, and the overall weight of evidence was for a beneficial effect from various kinds of acupuncture. Higher rigour studies are justified.

## Allergic rhinitis

In an early RCT, 102 participants with seasonal rhinitis were randomised to receive either genuine acupuncture to BL2, LI20 and LI4 or sham acupuncture subcutaneously over the patella (Williamson et al., 1996). Both interventions were given weekly for 3 or 4 weeks. Remission of symptoms was reported by 39% of the active treatment group and 45% of the controls, and a third of each group felt the treatment had had an excellent or very good effect. There was no significant difference between the two groups for any of the endpoints.

In a crossover study, 30 participants were given either acupuncture or sham acupuncture for 4 weeks, then crossed over to the other treatment without a washout period (Xue et al., 2002). Acupuncture was significantly superior on a five-point symptom scale, but there was no difference between groups for use of medication.

In a pragmatic RCT ( $n=981$ ) in Germany, a course of 15 sessions of acupuncture was compared with usual care for allergic rhinitis (Brinkhaus et al., 2008). Symptoms were evaluated with the Rhinitis Quality of Life Questionnaire (RQLQ). After 3 months, the RQLQ improved from a baseline of about 2.9 by mean 1.5 (SE 0.06) in the acupuncture group and by 0.50 (0.06) in the control group ( $P<0.001$ ). Moreover, quality of life improvements were more pronounced in the acupuncture than the control group.

The incremental cost-effectiveness ratio (ICER) was €17377 per quality-adjusted life year (QALY), which is well within the usual threshold for cost-effectiveness (Witt et al., 2009).

A large multicentre, sham-controlled RCT (ACUSAR) included 422 participants with seasonal allergic rhinitis and IgE sensitization to birch and grass pollen (Brinkhaus et al., 2010). Acupuncture plus rescue antihistamine medication (cetirizine) was compared with sham

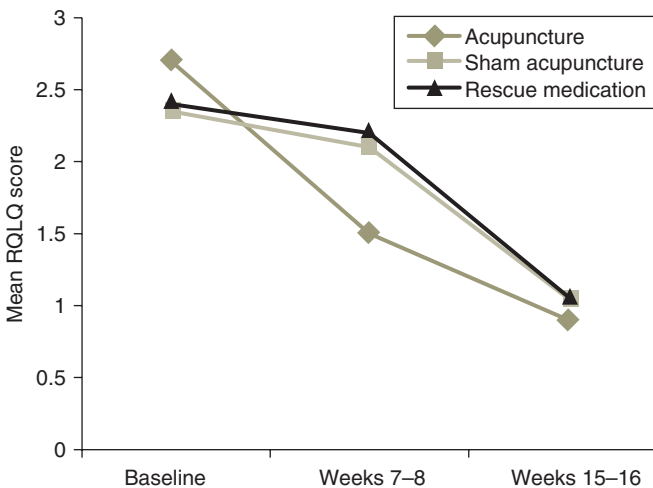
acupuncture (superficial insertion at non-points) plus cetirizine or cetirizine alone. Twelve acupuncture treatments lasting 20–30 min were provided over 8 weeks in year one. In the real acupuncture group, an average of 16 acupuncture points were used on an individual basis according to TCM theory and stimulated to achieve *de qi*. Obligatory points included LI4, LI11, LI20 bilaterally and Taiyang; at least three of Shangyingxiang, GB20, LR3, LU7, ST36, SP6, TE17 and BL13; and at least three additional points. The sham acupuncture group had needles inserted superficially in 5 of 7 predefined non-acupuncture points bilaterally without stimulation or *de qi*. The patients in the medication only group were given real acupuncture after the initial 8 week treatment period. Rescue medication consisted of up to two doses of cetirizine 10 mg daily, and if symptoms were not adequately controlled, then oral corticosteroids could be used in addition.

Primary outcomes were RQLQ and need for medication which they called rescue medication score (RMS). Outcomes were measured at 7–8 weeks after onset of treatment, at 16 weeks, and also the following year.

RQLQ decreased significantly more in the real acupuncture group than both other groups at the end of 7–8 week period, shown in Figure 29.1. This was the effect of acupuncture, not medication, since RMS also decreased by more in the acupuncture group than both other groups. At 16 weeks the differences were smaller and no longer statistically significant. The acupuncture group showed significantly better scores than sham in the following season, but not compared with the RM group which had also received real acupuncture by then.

The fact that acupuncture gave better symptomatic relief over and above the effect of these medications suggests that acupuncture is a viable therapeutic modality in the management of seasonal allergic rhinitis. However, the cost-effectiveness analysis showed an ICER for real acupuncture compared with cetirizine of between €31 241 and €118 889 from society's perspective and between €20 807 and €74 585 from a third party payer's perspective. On the basis threshold of €50 000 per QALY gained, the probability of additional acupuncture being worthwhile is very low, 1.3% or 22.2% respectively.

Therefore, acupuncture is effective treatment for allergic rhinitis and cost-effective against usual care though not in addition to cetirizine. It is therefore difficult to justify acupuncture's routine use for a self-limiting condition which resolves at the end of the season. However, acupuncture



**Figure 29.1** Effect of acupuncture on rhinitis symptoms as measured in the ACUSAR study (Brinkhaus et al., 2010).

is indicated for cases of allergic rhinitis where medication alone gives inadequate relief and may avoid the use of corticosteroids and their associated side-effects.

### Clinical points

Moderate evidence suggests acupuncture is an effective treatment for allergic rhinitis and recommended when medication is unsuitable.

Possible mechanisms of action of acupuncture for allergic rhinitis include a local reflex effect of needling on nasal airflow, demonstrated by rhinomanometry measurements (Sertel et al., 2009), and effects on the immune system (Carlsson and Wallengren, 2010) including the reduction of allergen-induced basophil activation (Pfab et al., 2011) and reduction of itch and flare response (Pfab et al., 2010), as discussed in Chapter 31.

Regular acupressure, using sustained stimulation of auricular points, or self-acupuncture may have advantages over intermittent sessions of acupuncture treatment. A systematic review found five RCTs, mostly at risk of bias, and concluded that acupuncture seemed more effective than herbal medicine, as effective as body acupuncture or antihistamine for short-term effect, and more effective than antihistamine for long-term effect (Zhang et al., 2010).

## Chronic rhinitis

Chronic rhinitis, also known as vasomotor rhinitis, is a non-allergic and non-infectious chronic disease that is accompanied by nasal hyperaemia and rhinorrhoea but without an increase in the number of eosinophils. It is more prevalent than allergic rhinitis, but the effect of acupuncture is little researched.

In a small RCT, 24 patients with a confirmed diagnosis of vasomotor rhinitis were randomly allocated to either acupuncture or sham laser acupuncture treatment (Fleckenstein et al., 2009b). Both treatments were given to five basic points (CV17, GV14, BL13, LI4, LI20, Yintang) plus any individually indicated points (GV20, GV23, SP6, LU7, ST36). Both were given weekly for 5 weeks. The main outcome measure was change in nasal sickness score (NSS; score max 27 points). This was significantly reduced in the acupuncture group from 9.3 (SD 3.9) to 4.1 (SD 3.2) points, and in the sham group from 5.6 (2.7) to 3.7 (2.6), which was a significant difference ( $p < 0.05$ ) even allowing for the baseline difference.

These results are promising, and further studies are justified.

## Chronic sinusitis

The symptoms of chronic sinusitis overlap with chronic rhinitis and the diagnostic criteria are not standardised, potentially causing confusion.

In a randomised comparison between deep and superficial needling, 16 patients with chronic sinus pain had five sessions of needling, the initial intervention being chosen at random (Lundeberg et al., 1988). The points used were GB14, BL2, GV23, SI18, LI20 and Yintang. Assessment of pain was made by VAS pain score, verbal rating and continuous graphic rating. Deep needling produced pain relief in 10 subjects whereas only five were relieved after superficial needling.

Another RCT included 65 adults with sinusitis symptoms for more than 3 months and evidence of sinus swelling, fluid or opacity on CT scan (Rossberg et al., 2005). Participants were randomised to (a) conventional care with decongestants, sodium chloride solutions and oral corticosteroids plus antibiotics as needed; (b) acupuncture according to traditional diagnosis or (c) minimal acupuncture to sham points avoiding the head and neck. Ten sessions of acupuncture or sham were given over 4 weeks. Outcome was assessed by CT scan, symptoms and quality of life. All groups improved somewhat, but by 4 weeks, conventional treatment was significantly superior by CT scan and showed a marked but non-significant trend towards being superior for symptoms and quality of life.

## Facial pain

Temporomandibular pain and trigeminal neuralgia are discussed in [Chapter 38](#). Persistent idiopathic facial pain, previously known as atypical facial pain, is described as a persistent facial pain that does not have the classical characteristics of cranial neuralgias and for which there is no obvious cause ([Cornelissen et al., 2009](#)). There exist very few reports of acupuncture for this indication, though therapeutic reviews mention the importance of a ‘multidisciplinary approach’.

Sixteen patients who had facial pain (mainly labelled as ‘atypical facial pain’) for more than a year were included in a crossover trial ([Hansen and Hansen, 1983](#)). Points appropriate to the affected division of the trigeminal nerve were selected: in the case of the first division, GB14, Taiyang and TE5; for the second division ST2, ST3 and LI4; and for the third division ST6, ST7 and ST45. Genuine treatment consisted of deep needling with *de qi*, and sham needling was performed by superficial insertion a short distance away from the correct points. Treatments were given for daily for 10 days with a washout period of 4 weeks between courses. Intensity of facial pain was scored by subjects in comparison with their usual level. The reduction in pain scores after acupuncture was significantly greater than that after sham.

## Bell's palsy

Bell's palsy is a rapid-onset facial nerve paresis or paralysis of unknown cause which usually recovers completely with time ([Baugh et al., 2013](#)). Oral prednisolone has some benefit in increasing recovery.

A Cochrane review of acupuncture for Bell's palsy was inconclusive because no studies reported the outcome that had been prespecified by the review – persisting sequelae at 6 months ([Chen et al., 2010](#)).

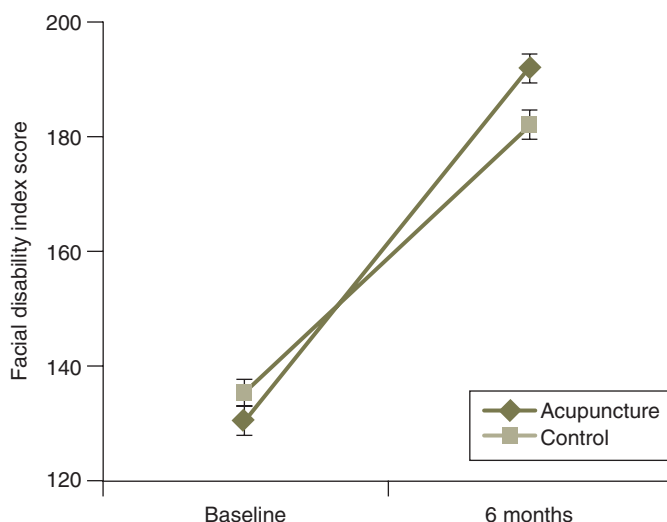
A second review found eight RCTs that measured response rates in a total of 10 comparisons ([Kim et al., 2012b](#)). Six found a higher responder rate with acupuncture and drug therapy compared to drug therapy alone ( $n=512$ , risk ratio (*RR*) = 1.11, 95% CI: 1.05–1.17;  $P=0.001$ ). Four found a higher response rate with acupuncture than with drug therapy alone ( $n=463$ ,  $RR=1.07$ , 95% CI: 1.02–1.13;  $P=0.006$ ). The risk of bias led to this evidence being described as ‘limited’ and so firm conclusions could not be drawn till further rigorous studies were conducted.

A multicentre RCT in China included 338 adults with a diagnosis of Bell's palsy in the last 4 days ([Xu et al., 2013](#)). The study was designed to test the effect of *de qi*, but also provides evidence of a ‘dose’ effect of acupuncture. Points used were GB14, ST4, ST6, ST7, TE17 on the affected side, and contralateral LI4. One group had strong manual stimulation to elicit *de qi*, the other no stimulation; needles were retained for 30 min. All patients were also prescribed prednisolone at a starting dose of 30 mg day<sup>-1</sup>. The main outcome after 6 months was facial movement graded by blinded assessors. Patients in the *de qi* group had significantly better facial function, as well as better disability assessment and better quality of life ([Fig. 29.2](#)).

Li and colleagues used fMRI to compare brain responses to acupuncture in patients with Bell's palsy at different pathological stages with normal controls and found that the response to acupuncture varied at different pathological stages of Bell's palsy, though this finding may not be linked to the mechanism of action ([Li et al., 2013](#)).

## Sore throat

Sixty patients with acute tonsillitis and pharyngitis were enrolled in a placebo-controlled RCT ([Fleckenstein et al., 2009a](#)). They received either acupuncture or sham laser acupuncture to the LI meridian between acupuncture points LI8 and LI10. The main outcome measure was the change of pain intensity on swallowing a sip of water 15 min after treatment. The pain scores for the



**Figure 29.2** Effect of acupuncture on Bell's palsy assessed using facial disability index score (Xu et al., 2013).

acupuncture group fell from mean 5.6 to 3.0 (SD  $\pm$  3.0) and for the sham group from 5.6 to 3.8, a difference that was not significant. Patients' satisfaction was high in both treatment groups. The study was terminated prematurely due to a lack of suitable patients.

A series of clinical trials found evidence that bilateral acupuncture to the 'Y' points (Yoneyama, a fingerbreadth lateral to the midline) could reduce the symptoms of sore throat compared with no treatment (Kawakita et al., 2008).

## Common cold prevention

Prevention of the common cold has been a popular subject for research in Japan, including some small RCTs in one centre, a review of which reported no evidence of benefit overall (Kawakita et al., 2008). A wider review found six RCTs, five of which showed acupuncture superior to no acupuncture, but the quality of studies was low (Suzuki et al., 2009).

## Concluding comments

In summary, the balance of evidence suggests that acupuncture can be effective in the treatment of motion sickness, Bell's palsy – and allergic rhinitis, where it is not cost-effective in relation to medication, though a useful option when drugs are unsuitable. Acupuncture may be helpful in treating dizziness associated with neck muscle tension, Meniere's disease, and persistent idiopathic facial pain. The effect on chronic (vasomotor) rhinitis is uncertain, and it is also not clear whether acupuncture has any effect as an adjunct in the management of tinnitus or vertigo. It may relieve acute sore throat, but its effect on prevention of the common cold is uncertain. The balance of evidence suggests it is of no benefit for chronic sinusitis and cannot alleviate sensorineural deafness.

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# Acupuncture for eye conditions

E. Rom

## CHAPTER OUTLINE

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## Introduction

The ophthalmology department is not the first place that comes to mind when thinking of acupuncture, at least not in the English-speaking world. There is increasing evidence that sensory stimulation in the form of acupuncture or acupressure may have some potential in pain management, regulation of blood flow, neuroprotection and pro-homoeostatic processes. Despite significant progress with new drugs and more advanced surgical techniques in management, some common eye diseases may still leave some patients potentially visually impaired. Blindness carries with it an existential psychological threat. All reasonable approaches to reduce the risk of blindness need to be scientifically evaluated. Patients are willing to explore almost any avenue, the orthodox medical practitioner being just one point of reference amongst others. In US surveys, the prevalence of patients admitting to concomitant treatment with acupuncture were 1.9% (Rhee et al., 2002) and 1.8% (Wan et al., 2012) in a tertiary referral centre for glaucoma clinic, 24% in the uveitis clinic (Smith et al., 2004).

Systematic reviews suggest that few high quality trials have been conducted for acupuncture in ophthalmology. An exception is the clinical controlled trial by Kim et al. (2012) on acupuncture for dry eyes. Lack of evidence of effect, however, is not evidence of lack of effect. The following account is an attempt to draw together the available evidence relevant to the practitioner using acupuncture in eye care.

## Advantages, disadvantages and dangers of acupuncture

The *advantages* of the complex intervention of acupuncture are obvious. Provided there is a clear diagnosis, the practitioner is knowledgeable of the anatomy, the natural history of the condition and the implications for the affected person and of other treatment strategies, acupuncture is safe. It is inexpensive and low-cost. It would therefore also be useful for preventative health care and in low-income settings. It may encourage the practitioner to think ‘outside the box’.

The main *disadvantage* of acupuncture consists of potentially inflated expectations of the patient. They leave the door open to both emotional and financial abuse of patients disappointed with conventional health care. In Germany, patients have been known to sell the family silver in order to pay for acupuncture treatment courses that were unlikely to be successful in their situation and often given by practitioners with doubtful qualifications.

Neither the optimum treatment schedule nor the expected effect size are known. Suggestions on treatment plans can be derived from physiology, from other clinical specialties e.g. stroke research, dermatology, and where available from laboratory research or traditional Chinese protocols for the time being. Clearly there is the need for more research.

Acupuncture also brings with it some potential dangers. Without an orthodox diagnosis, acupuncture may delay treatments (Peuker and Gronemeyer, 2001) which have proven to be sight-saving (e.g. in retinal detachment, corneal ulcer, glaucoma, thyroid eye disease) or could have prevented complications (vascular occlusions). Traditional Chinese medicine (TCM) was developed before the invention of the ophthalmoscope, and many eye conditions are insufficiently described in their complexity in the classical texts (Kovacs and Unschuld, 1999).

Local and peripheral acupuncture can increase the blood flow to the eyes, in particular where there is active eye disease (Naruse et al., 2000; Litscher and Schikora, 2002; Litscher et al., 1999; Nientzow et al., 2006; Takayama et al., 2012). Acupuncture may therefore trigger intraocular bleeding when there are abnormal blood vessels, e.g. wet age-related macular degeneration (ARMD), or proliferative diabetic retinopathy. The presence of pathological blood vessels should be excluded before treatment and should be monitored periodically (Kuestermann, 2006).

Ocular perforation with the acupuncture needle is a rare but documented complication with potentially devastating consequences leading to loss of sight or eye/blindness through infection (endophthalmitis), haemorrhage or retinal detachment (Fielden et al., 2011). Damage to intraorbital blood vessels may theoretically lead to retrobulbar haemorrhage especially if there was needle manipulation within the orbit. Retrobulbar haemorrhage is one of the few true emergencies in ophthalmology, which must be recognised immediately by the practitioner. Even the microsystem of ‘eye acupuncture’ described by Fu (1991) recommends that the needles are placed outside the orbital margins on the periosteum of facial bones.

## Commonly used points for eye conditions

### Local/proximal points

There are plenty of local points which can be used safely and which have shown to give an effect on the eyes. They are often used in combination with distal points (Wei et al., 2011b). Local points included in most studies (Table 30.1) stimulate structures within the distribution of the trigeminal nerve or C2. Most of them are related to fibro-neuro-vascular bundles (Shaw, 2013). As the face is highly vascularised, local points are slightly more likely to cause some bruising than needling of other areas.

### Distal points

Sensory stimulation at the major acupuncture points has been shown to have effects on the autonomic nervous system, the immune system and central effects. Eye conditions usually involve those systems as well. In TCM theory, all the channels are believed to have some connection to the

TABLE 30.1 ■ Local points and their innervation

Point	Nerve supply
BL2, Yuyao, Yintang	V1
ST2	V2
TW21, SI19	V1/2
BL10	C1–C5
GB20	C1–C3

TABLE 30.2 ■ Commonly used points and their innervation

Point	Nerve supply
LR2, LR3	L4–S3
ST36, SP6	L4/5–S2
LI4, LI11	C5–T1
GB37	L5–S2
KI3	L4–S2

eye (Wang and Robertson, 2008). Combining a modern neurophysiological approach with these historical insights, the pooled experience can be used for the benefit of the patient. Distal points are often combined with local points (Table 30.2).

**Auricular points**

Recently there have been attempts at scientific explanations of or measurements of effects from auricular acupuncture (Alimi D. Auriculothérapie et cerveau. ASA-TCM Congress of the Schweizerische Gesellschaft fuer Traditionelle Chinesische Medizin presentation, Dec 2012; Oleson, 2003; Usichenko et al., 2010; Chung et al., 2011).

Clinical evidence suggests the potential of auricular acupuncture for a range of eye and facial conditions, from dry eye disease, to facial pain including trigeminal neuralgia and other neuropathic pain and temporomandibular disorder, to recurrent corneal erosion syndrome, resistant to any other treatment. The method of finding the ‘very point’ (Gleditsch, 1995), or noticing the ‘grimace-sign’ (Bahr, 2012) appears to give the best results, rather than locating the insertion site from charts. For frequent treatment, the points should be rotated so as to avoid the development of allodynia.

**Other microsystems.** In Germany and Switzerland the microsystem approach developed by the Dane Jan Boel, ‘acupuncture 2000’ (Boel, 2007) is popular. The standardised protocol entails needling of fixed points around the joints of fingers and feet twice daily over 5 days for 2 weeks with a technique resembling the ‘very point’ technique of Gleditsch. Although it would lend itself to a randomised controlled trial, none could be found in the literature. In practice, the method appears to be used in combination with other local and distal points (Table 30.3).

TABLE 30.3 ■ Points used in Boel Protocol, after Krenn (2006)

Acupuncture points	
Session 1	Yintang, Yuyao, BL2, auricular point of cervical vertebra, Dahlgren, ECIWO eye point
Session 2	BL67, BL60, ST36, LR3, auricular point liver

## Anterior segment conditions

### CONJUNCTIVA AND EYE LIDS

The soft tissues around the eyes, lids and conjunctivae are commonly involved in infectious, inflammatory and allergic conditions. The condition most commonly seen by generalists is probably infectious conjunctivitis, followed by keratoconjunctivitis sicca. For chronic and frequently recurring conjunctivitis, chlamydial conjunctivitis needs to be excluded as it always requires systemic treatment of both the patients, and their partners, in addition to local antibiotics.

### INFECTIOUS CONJUNCTIVITIS

This common, generally self-limiting condition is usually treated with antibiotic eye drops. This is therapeutic for bacterial conjunctivitis and prophylactic to prevent bacterial superinfection in viral conjunctivitis. Lubrication provided by the antibiotic eye drops will also make the eyes feel more comfortable.

Deng describes the outcome of 60 patients with what they called ‘fulminant red eye’ with systemic features, probably *bilateral viral conjunctivitis* (Deng, 1985). Thirty patients were treated daily with acupuncture to bilateral *Taiyang* and BL2 and letting of 4–5 drops from tender ear points on a daily basis, together with 0.25% chloromycetin eye drops 4 hourly. The remaining 30 received antibiotic drops only. The acupuncture-treated group is reported to have had immediate relief from their systemic and ocular complaint and to have experienced full recovery within half the time of the ‘eyedrop-only-group’. The ‘blood letting’ treatment surely is of historical interest only.

There is no consensus amongst German ophthalmologists on the use of acupuncture in infectious conjunctivitis (Ots, 2006): Schellenberg, an experienced paediatrician, routinely offers parents of infants and toddlers with conjunctivitis the choice between one uncomfortable short treatment which will make the child cry for a few minutes or 4–5 days of three times daily instillation of drops – which most likely will make the child cry three times daily for 4–5 days. Schellenberg is reported as using LR3 bilaterally for 5 s, not too gently, LI11 on one side, and GV14, while the child is in the carer’s arms. In his experience this two-minute treatment often clears the condition. This anecdotal report has not been supported by a published audit or independent observations.

### Allergic eye disease

There are two forms of this disease which can affect the eyes and surrounding tissues asymmetrically. The most common form, *simple allergic conjunctivitis*, is self-limiting; but as *vernal keratoconjunctivitis*, allergic conjunctivitis tends to run a chronic course and can lead to severe complications. Orthodox treatment may include steroids and/or immunosuppressants. No reports of acupuncture trials have been found.

### DRY EYE DISEASE

This multifactorial, complex disease is only rarely sight-threatening (Massof and McDonnell, 2012; Lemp, 2007, 2008). However, the patient is uncomfortable all the time. The quality of life (QoL) of moderate to severe dry eye is compared to QoL of moderate to severe angina (Schiffman et al., 2003). The Ocular Disease Surface Index, a validated questionnaire, reflects the patient experience better than any other clinical test (Caffrey, 2004). A poor precorneal tear film tends to be unstable and can paradoxically present as a watery eye. Lifestyle factors, in particular, diet, coffee consumption and hydration, nicotine abuse, lack of sleep and air humidity of home and workplace should be considered (Lemp and Foulks, 2007). Supplementation with vitamin C, E and omega-3 has been recommended (Eperjesi and Beatty, 2006). Once sinister causes of a painful red eye (e.g. cicatricial pemphigoid, Stevens–Johnson disease) and systemic associations (e.g. Sjögren’s

syndrome, rheumatoid arthritis, thyroid dysfunction) have been excluded, lifestyle adjustments, lubrication with artificial tears and punctal plugs are the first interventions. Acupuncture is recommended as a second line treatment strategy. A questionnaire before and after treatment can be useful as the improvement tends to be gradual.

The points commonly used are those around the eyes summed up in [Table 30.1](#). Many practitioners would use those points in combination with auricular and distal points, irrespective of the TCM diagnosis or in addition to the protocol prescribed by TCM theory, also using pulse and tongue diagnosis.

[Omata et al. \(2000\)](#) examined the effect of electroacupuncture (EA) on lacrimation and salivation. In 10 normal controls EA with 1 Hz to the posterior neck and upper scapula had no effect. 1/30 Hz to the face increased lacrimation and salivation. In 15 patients with Sjogren's syndrome, 1/30 Hz EA to the face increased lacrimation and salivation: there was no effect in seven patients 0, 30, 60 or 120 min after treatment; but 10 patients with Sjogren's syndrome experienced increasingly significantly improved salivation during the course of 10 sessions of EA in the face (English abstract from the authors, article in Japanese). Patients should be advised of a delayed response.

In 2002, Niemtzow et al. described a protocol for xerophthalmia and xerostomia for patients after radiotherapy ([Niemtzow et al., 2002](#)). Salivation responded better than lacrimation. They used ear points: *Shenmen*, zero and salivary gland and bilateral LI29, a new point on the LI channel just proximal to LI1. [Grönlund et al. \(2004\)](#) randomised 25 patients to either acupuncture or artificial tears. After 10 treatment sessions, 1–2× per week, there was a significant subjective improvement after 2–3 weeks, but that had worn off at 8 months. Points used were ST2, ST8, ST36, GB1, GB14, BL2, LI4. An audit project on 52 patients showed that treatment can be effective after one session ([Rom, 2009](#)). Most patients said that the effect lasted for 6–8 weeks. After 3 months the effect had usually worn off. The protocol combined local, distal and ear points. A German translation of the ocular surface disease index questionnaire was the primary outcome measure. Sessions can be scheduled weekly initially until improvement is reported.

[Nepp and Wedrich \(1994\)](#) initially analysed the relevance of Chinese pattern diagnosis in dry eye disease. Later, they came to the conclusion that patients are more symptomatic when under psychological stress. They suggested that the more prominent the psychological factors are, the more likely that acupuncture will help as both are mediated through the autonomic nervous system ([Nepp et al., 2000](#)). The combination of acupuncture with psychoanalytical or hypnotic intervention has also been reported by other practitioners in Germany ([Schweizer-Arau, 2011](#)). Fossion suggests that the peripheral points ST36, LR3 and GB34 stimulate the subparafascicular and parabrachial nucleus in the brainstem and thereby indirectly the superior salivary nucleus. This nucleus influences lacrimation through cholinergic nerves. From this pattern of innervation he hypothesises a correlation of TCM patterns related to autonomic innervation of head and neck and a rationale for the use of peripheral points. [Ventura \(2009\)](#) summarises the hypothesis that acupuncture is beneficial in dry eyes through up-regulation of the parasympathetic system ([Ventura, 2009](#)). Significantly, cholinergic nerves have been found in the anterior segment of the eye ([Liu et al., 2007](#)).

While the systematic review on acupuncture for dry eye by [Lee et al. \(2011\)](#) concluded that there was 'no firm evidence' ([Lee et al., 2011](#)), the subsequent RCT by [Kim et al. \(2012\)](#) ( $n = 150$ ) compared the results of acupuncture (bilateral BL2, GB14, TE23, Ex1, ST1, GB20, LI4, LI11 and GV23) three times per week over 4 weeks with artificial tears once daily. The effect of acupuncture was not inferior to conventional lubrication but the effect was of longer duration.

## UVEITIS

This inflammation of the vascular coat of the eye may present clinically as a painful, red eye, with photophobia, most often unilateral. Background investigations of the most common form, the 'idiopathic anterior uveitis', rarely reveal any significant aetiology.

When recurring uveitis is a complication of Behcet's disease, it can be sight-threatening. Yu et al. found in a group of 20 patients that acupuncture reduced the recurrences of uveitis compared to the controls who had 'usual care' only. They measured the kappa chains of IgM and the blood zinc levels. Both differed significantly between acupuncture-treated and non-acupuncture-treated patients (Yu et al., 2001, 2003, English abstract, article in Chinese).

## CATARACT

The crystalline lens of the eye gradually opacifies with age. Operative cataract removal with intraocular lens implant is a very successful treatment with a low complication rate. In 1996, Cui reported 62 cases of symptomatic cataract treated with ear acupuncture (Cui, 1996). The claims of regression of cataract as documented by improved visual acuity and/or reduced lens opacity on ophthalmoscopy in 56 cases (90.33%) after one to three courses of intensive 10-day treatments with ear acupuncture in humans had appeared unlikely and was initially disregarded. Then, Cariello et al. (2006) induced cataract in the eyes of 80 Wistar rats with selenite injections, the standard animal model for cataract. 20 rats served as observation group only (100% no cataract). The treated animals were randomised into four groups, and EA produced a highly significant ( $p < 0.001$ ) reduction in cataract formation (Fig. 30.1). Larger and randomised clinical trials are clearly required.

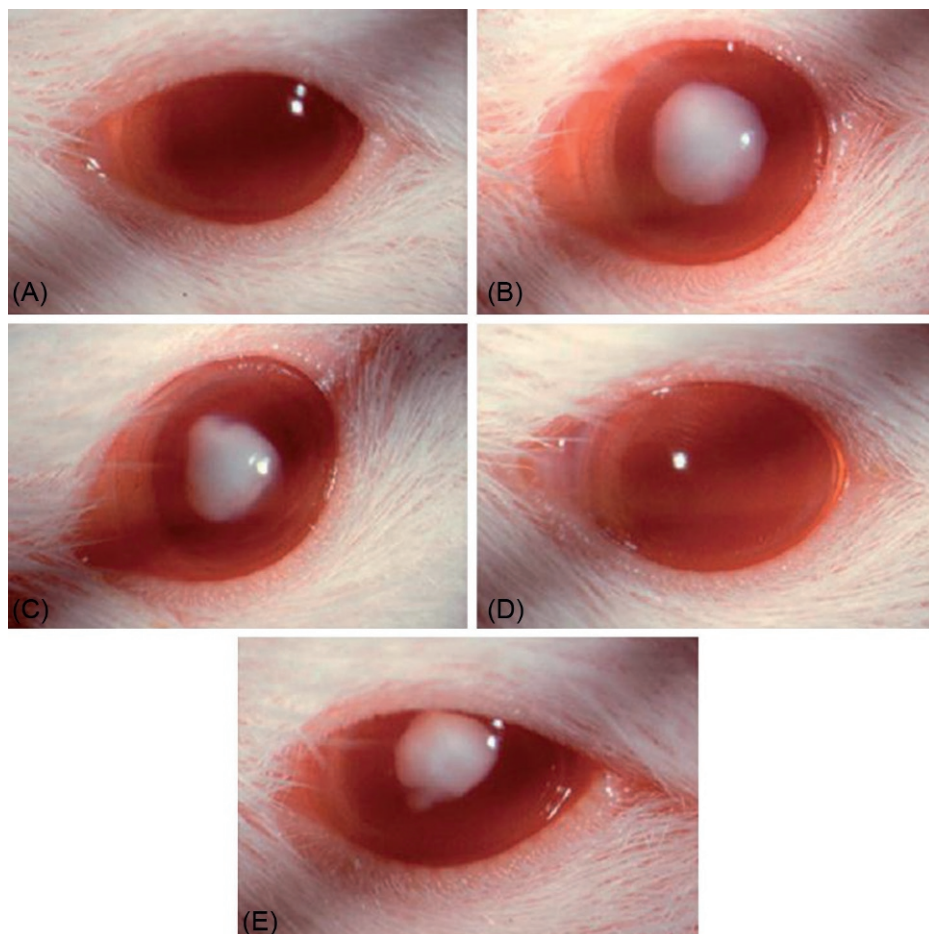
## BLEPHAROSPASM, BELL'S PALSY AND THYROID RELATED OPHTHALMOPATHY

These are not strictly ophthalmic conditions. Blepharospasm may lead to functional blindness as the patient cannot see while the eyelids are closed. Idiopathic VII cranial nerve (Bell's) palsy and dysthyroid eye disease also affect the ocular surface. This surface disturbance is the most likely aspect that may respond to acupuncture. There are only anecdotal reports with mixed results. Systematic reviews concluded that there was not enough evidence to make firm recommendations (Rogvi-Hansen and Perrild, 1991; Story, 1989; Wu et al., 1985; Zhou et al., 2009; Chen et al., 2010).

## POSTHERPETIC NEURALGIA

This feared long-term complication of herpes zoster occurs more commonly in the ophthalmic form than in other locations (Wood et al., 1996) and is the more common the older the person is. Other complications include chronic uveitis and secondary glaucoma which require orthodox treatment. In the very early stages, systemic antiviral medication is indicated. Acupuncture in the form of 'surrounding the dragon', including EA, combined with some general points may reduce pain in the acute phase and prevent the development of neuropathic pain. The postherpetic neuralgia is thought to be associated with upregulated TRPV1, the transient receptor potential vanilloid one receptor targeted by capsaicin (Webster et al., 2010). Capsaicin has been used successfully topically for post-herpetic neuralgia (PHN), has been shown to deplete substance P (Wood et al., 1996) but may lead to hypaesthesia after repeated applications (Tontodonati et al., 2012) through atrophy of the nerve cells. TRPVN1 expression has been shown to be upregulated after EA (Abraham et al., 2011).

The initial reports of use of acupuncture for postherpetic neuropathic pain by Lewith and Field in 1983 (Lewith and Field, 1980) was inconclusive; reports by Coghlan (1992) and He and Fang (2007) and anecdotal experience, while methodologically flawed, have been encouraging. A systematic review considered acupuncture for PHN as 'not yet adequately tested rather than demonstrating no evidence of efficacy' (Hempenstall et al., 2005). Recently Ursini et al. (2011) reported on the results of a prospective, randomised trial ( $n = 102$ ) comparing pain control in patients with herpes zoster on standard pain treatment (pregabalin, local injections of chirocaine alternate



**Figure 30.1** Acupuncture for cataract prevention. Animal model of cataract induction by subcutaneous selenite injection. (A) Control group: no cataract. (B) Selenite injection: 100% cataract grade 4–6. (C) Selenite and anaesthesia: 100% cataract grade 4–5. (D) Selenite and EA under anaesthesia: 45% no cataract, 20% cataract grade 1–3, 35% grade 4–5. (E) Selenite and sham acupuncture under anaesthesia: 100% cataract grade 4–5 (Cariello et al., 2006).

days, plus transdermal buprenorphine or oral oxycodone up to 400 mg daily) to patients with eight sessions of individualised acupuncture twice per week as pain control. Paracetamol was allowed as rescue medication in both groups. There was no difference in pain levels or development of PHN at 3 months or 1 year. Clinical experience suggests that the later the patient presents, the less likely it is that the neuropathy will respond to acupuncture.

## MYOPIA, HYPERMETROPIA, AMBLYOPIA AND SQUINT

Use of acupuncture for emmetropia, in particular myopia, is widespread in China. Anecdotal reports mainly stem from the 1980s (Chen, 1989; Ribaute, 1987). A Cochrane review found 35 trials on the subject of myopia prevention (Wei et al., 2011a). Only two met the inclusion criteria: Those included 131 children. Both groups used auricular acupuncture combined with a second

intervention as control (multimedia interactive education, [Yeh et al., 2008](#)), atropine 0.25% and 0.5% ([Liang et al., 2008](#)). Neither a conclusion nor treatment recommendation was made in the review. The observed small effects may be due to relaxed accommodation through parasympathetic activation from the ear acupuncture. No measurements of the axial length were made. The often mentioned ‘eye exercises’ for myopia appear to relieve asthenopic complaints but not to influence refractive errors ([Östberg et al., 1992](#)).

Anisometropic amblyopia was the subject under investigation in a study on 83 children ([Zhao et al., 2010](#)). Intensive acupuncture treatment (five sessions per week over 8 weeks) was compared with, possibly sub-optimal ([Lam et al., 2011](#)), occlusion therapy for 2 h daily, applied by the parents, monitored by four clinic visits. The authors described a mean improvement at 15 weeks of 2.2 lines in the occlusion group versus a 2.9 line improvement in the acupuncture group, which was considered to be equivalent. An intense discussion ([Leguire, 2011](#); [Barclay, 2010](#); [Zhao et al., 2010](#)) followed, mainly about the methodology and possible bias. That was followed by the expected conclusion that more research is required. Also the meta-analysis of 14 trials involving 2662 participants after search of Western and Chinese databases by [Yan et al. \(2013\)](#), concluded that there may be a suggesting that acupuncture may be favourable but that more research was needed.

## THE GLAUCOMAS

‘Primary angle-closure glaucoma is an ophthalmic emergency’ ([Wei et al., 2011b](#)). Immediate consultation of an ophthalmologist is needed. TCM colleagues from Chengdu TCM University at a Sino-German research meeting in Berlin 2010 were united in their opinion that narrow-angle glaucoma should be treated by orthodox medicine. Presumably, they were wary about treating glaucoma at all, because in China narrow-angle glaucoma is the most common form. There is no justification for delaying access to orthodox treatment (laser with or without surgery). Irreversible blindness can occur within hours in the acute form. Perhaps, it may be possible to bridge the time (more likely to be hours than days) with drugs and acupuncture until the definitive treatment can be arranged (laser treatment or surgery). Acupuncture cannot ever be a substitute for orthodox treatment in this situation.

Open-angle glaucoma, in contrast, is a group of optic neuropathies with a typical optic nerve appearance, progressive visual field defects, abnormal regulation of blood flow to the optic nerve and an increased rate of apoptosis (programmed cell death) of the retinal ganglion cells ([Almasieh et al., 2012](#); [Flammer and Mozaffarieh, 2007, 2008](#); [Pascale et al., 2012](#); [Quigley, 2011](#)). Open-angle glaucoma often shows features of systemic involvement, including autonomic dysregulation ([Gherghel, 2004](#); [Gherghel et al., 2004](#); [Pache and Flammer, 2006](#); [Wostyn et al., 2010](#)). Lowering the intraocular pressure (IOP) is the mainstay of pharmacological and surgical treatment with the aim of preventing blindness ([Anderson et al., 2003](#); [Caprioli and Varma, 2011](#); [Heijl et al., 2002](#)). Professor Qi-Ping Wei, Beijing, reported studies on point specificity in patients with glaucoma using so-called ‘source’ points, but found the results disappointing ([Wei et al., 2011b](#)). Multiple small-scale studies indicate that acupuncture and acupressure may lower IOP ([Ewert and Schwanitz, 2008](#); [Her et al., 2010](#)), increase the blood flow to the eye ([Kurusu et al., 2005](#); [Litscher, 2007](#); [Litscher et al., 1999](#); [Takayama et al., 2011](#)) and play a role in neuroprotection of the retinal ganglion cells ([Chan et al., 2005](#); [Pagani et al., 2006](#)). This is an area where more research is required and acupuncture may well take a prominent place in the future ([Rom, 2013](#)).

## Posterior segment conditions

### AGE-RELATED MACULAR DEGENERATION

ARMD is the third most common cause for blindness worldwide. It is multifactorial, accompanied by abnormal circulation in the choriocapillaries, by formation of drusen with deposition of lipids,

lipofuscin, amyloid at the level of Bruchs membrane (Miller, 2013; De Jong, 2000). An increased rigidity of the sclera has been observed, as also an increase of inflammation (Seddon et al., 2004; Vine et al., 2005) which appears to be correlated to the vascular endothelial growth factor (VEGF) (Jackson et al., 1997). There are two forms of ARMD, a dry form and a wet form. The insidious dry form shows atrophic patches, 'geographic' degeneration of the retinal pigment epithelium leading to loss of neuroretina. No treatment is clinically in use for this form as yet (AMD Guidelines Group, 2013).

The wet form is characterised clinically by distortion of vision (metamorphopsia), morphologically by neovascularisation, subretinal fluid, exudates and haemorrhage. New treatments with intravitreal injections of anti-VEGF medication have revolutionised the conventional treatment options since about 2008 with good results. In active wet ARMD the C-reactive protein is increased (Kikuchi et al., 2007). It is therefore conceivable that the immune-modulating and anti-inflammatory effect of acupuncture could be harnessed before the macular degeneration becomes wet. As there is a proliferative element in the subretinal neovascular membrane, acupuncture in this acute stage may potentially lead to acute haemorrhage through increased blood flow. In a personal communication, Professor Wei does not recommend the use of acupuncture in the acute stage for this condition (Wei, 2011). Several German practitioners report improvement in visual acuity in a significant number of patients with exudative scars (Paeraermann, 2011). Most combine treatment according to Boel with TCM and other complementary methods. The available anecdotal reports (Wegschneider, 2012) and case series (Krenn, 2008; Lundgren, 2003, 2005, 2008) suggest that some patients with dry and non-active wet ARMD may benefit from acupuncture (Table 30.4).

RETINITIS PIGMENTOSA

Pagani et al. (2006) show graphically the neuroprotective effect of acupuncture on Royal College of Surgeon rats which have the genetic defect to develop blindness due to retinitis pigmentosa (RP). After treating the rats with EA from day 30 to 41 of their life during the sensitive period of the eye's development, the retinae of the treated rats look more normal histologically, show less ischaemia; and the profile of nerve growth factors and their receptors are altered. This suggests

TABLE 30.4 ■ Case series of acupuncture for AMD

Reference <i>n</i> , indication	Method	Results
Anecdotal Wegschneider (2012), <i>n</i> = 23, dry and wet AMD	TCM and Boel Individualised, some herbs	70% improved or stable
Krenn (2008), <i>n</i> = 328, dry AMD	Boel 2x daily for 5 days for 2 weeks	Distance vision: 44.2% improved, 51.5% stable, 4.3% deterioration. Near vision: 88.4% improved, 8.8% stable, 2.7% deteriorated
Lundgren (2003, 2005, 2008), <i>n</i> = 268, dry AMD	EA around eyes and LR14, LR3, LR8, and auricular	88.1% improved, 9.6% continued deterioration
Lundgren (2003, 2005, 2008), <i>n</i> = 68, non-active wet AMD	Too complex to summarise	84.5% improved, 13.4% continued to deteriorate but no case of haemorrhage
Paeraermann (2011), <i>n</i> = 137, dry AMD	Individualised, homoeopathy, diet and oxygen therapy	94% improved

AMD, age-related macular degeneration.

the possibility that acupuncture may improve ocular vascularisation, reduce ischaemia, regulate ocular growth factors and, in short, have a neuroprotective effect on the retina. There are anecdotal reports of acupuncture improving the visual field defect in RP. Tian describes a combination of acupuncture (*Taiyang*, BL1, GB20, ST36, KI3 and LR3 or SP6 and GB37 for 30 min) with moxibustion of herbs (*Flos Chrysanthemi Indici* and *Fructus lycii*) close to the eyes for 15 min. A 62.5% success rate is claimed in the 40 cases (Tian, 1991).

Reddy and Fouzdar (1983) took 50 patients with variable diagnoses for whom no further conventional ophthalmic treatment was indicated because no known treatment would have influenced the course of the disease positively. Their standard protocol included retrobulbar Shangming and Qiuhou, segmental GB14, GV20 and distal LI4: 20 cases of RP had best results; 12 cases of optic atrophy showed some improvement; 10 cases with myopic degeneration, showed reduction of spectacle correction by 1–1.5 dioptres in 4; but eight cases with what was described as ‘macular choroiditis’ did not have encouraging responses. Despite the mixed results, they felt that it was right to offer treatment in order to give patients hope. The standard of reporting is typical for the era before introduction of evidence-based medicine in most countries at the beginning of the twenty-first century. Further research is clearly required.

## RHEGMATOGENOUS RETINAL DETACHMENT

This conditions needs to be managed surgically. The success rate after timely surgical retinal detachment repair is very high; some departments say up to 96%. Under no circumstances should surgical treatment be delayed. Only after-effects of the retinal detachment repair such as central retinopathy may or may not be accessible to acupuncture treatment via the anti-inflammatory effect of acupuncture. Expectations need to be managed in a responsible manner.

## CENTRAL SEROUS CHORIORETINOPATHY

This focal sensory macular detachment, thought to be caused by impaired choroidal autoregulation leading to hyperpermeability due to ‘stasis, ischemia or inflammation’ and/or retinal pigment epithelial dysfunction (Nicholson et al., 2013). Fluid collects between the sensory retina and the retinal pigment epithelium. It usually is self-limiting. The natural history of central serous chorioretinopathy (CSR or CSC) usually leads to spontaneous resolution within 6 months to 2 years with only a minority of patient being left with permanent visual disturbance. CSC affects men age 40–50 years more often than women. It can be associated amongst other factors with stress (type-A personality, Yannuzzi, 1987), hypertension, autoimmune conditions and steroid use.

In the macaque monkey it can be experimentally produced by adrenalin injection into the eye. This involvement of hormonal and autonomic influences (elevated corticosteroids and adrenalin in patients with CSC) may give a rationale for the use of acupuncture. It usually affects one eye and presents with blurred or distorted vision. Photodynamic therapy has shown some promise in orthodox treatment.

In 1987, Lu and Friberg reported 600 cases of CSC treated with a standard protocol of daily acupuncture to Xiangyang (between the hyoid bone and medial edge of the mandible) for 10 days (Lu and Friberg, 1987). If no resolution had occurred at completion of the treatment course, another course was offered. Eighty-six percent of patients had recovered at follow-up at 3 months, either through natural remission or acupuncture.

## OPTIC ATROPHY

In 1992, Dr Qi-Ping Wei summarises the results of 12 heretogeneous reports by various authors on 2647 eyes (Wei, 1992). A positive effect was found in 68.4% of patients (60.9–88.8%), treatment methods were variable, including combination of orthodox medicine (presumably steroids)

and acupuncture and herbal treatment. The results depended, according to his analysis, on (1) cause: traumatic cases respond better than idiopathic; (2) duration of condition: long-standing cases are less likely to respond; (3) age: patients under the age of 21 years are more likely to improve with treatment; (4) visual acuity before treatment, but even visual acuity of light perception is reported to respond occasionally; (5) duration of treatment: recommended treatment schedule is daily treatment for 7–10 days, 2–3 days rest over a period of 3–6 months.

Dai et al. (2013) included 13 RCTs involving 1180 eyes with optic atrophy in their meta-analysis and concluded that ‘the effect of acupuncture combined with medicine was superior to medicine alone’ (English abstract of Chinese article, full text not available in any European language).

The evidence is not conclusive. Access to original reports and further research would be required to reach a conclusion whether or not to even mention acupuncture to people with optic atrophy.

A novel technique from Japan, related to EA, called ‘transcorneal electrical stimulation’, has been investigated in an animal model of experimental optic atrophy. Electric current is applied via two concentric wires, representing the two electrodes, attached to the inner surface of a corneal contact lens. The 20 Hz biphasic square wave pulses were tested on rats after experimental crush injury of the optic nerve. Functional improvement was observed (Miyake et al., 2007). A small case series with patients with branch retinal vein occlusions used transcorneal electrical stimulation for 30 min once a month for 3 months; best corrected visual acuity, visual fields and electrophysiology (mfERG) suggested an effect (Inomata et al., 2007). A similar protocol comparing long-standing with recent cases of vein occlusion suggested, paradoxically, that the effect was greater in long-standing cases of retinal vein occlusion (Oono et al., 2011). Transcorneal electrical stimulation may have similar effects as EA to local extra-orbital points. Further investigation is required.

## Concluding comments

Studying the effect of acupuncture on the eyes may give new insight into disease processes and thereby help to prevent blindness. For acute sight-threatening conditions (retinal detachment, acute glaucoma, corneal ulcers), orthodox medicine is the treatment of choice. For chronic conditions (e.g. open-angle glaucoma, inflammatory conditions), acupuncture may be considered as a complementary treatment method. Acupuncture shows promise for keratoconjunctivitis sicca, or chronic progressive degenerative conditions. It may shorten the course of otherwise self-limiting conditions (uveitis, central serous retinopathy). For conditions with insufficient evidence, patients’ expectations need to be carefully managed. Professionalism, skill, experience and knowledge is required to avoid adverse events. Observational skills and an open mind may advance our understanding and expand the limits of our knowledge.

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# Acupuncture for skin conditions

F. Pfab

## CHAPTER OUTLINE

<b>Introduction</b>	<b>528</b>	<b>Raynaud's phenomenon</b>	<b>531</b>
<b>Experimental itch</b>	<b>528</b>	<b>Psoriasis</b>	<b>531</b>
<b>Nephrogenic itch</b>	<b>528</b>	<b>Other skin conditions</b>	<b>532</b>
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## Introduction

The skin as the primary insertion site of an acupuncture needle plays an essential role in the application of acupuncture. Archaeological and paleomedical investigations in mummies such as the Tyrolian iceman Ötzi point towards acupuncture point stimulations by tattooing the skin as long as several thousand years ago (Dorfer et al., 1998, 1999).

Although high quality acupuncture research in the field of dermatology has grown a lot within recent years it is still limited. Studies on skin conditions that are of an evidence-level grade I (randomised controlled trials (RCT) or meta-analysis) are discussed later.

## Experimental itch

Itch is the main symptom of skin diseases and defined as unpleasant sensation inducing the desire to scratch. Several studies have investigated the effect of acupuncture on itch in healthy volunteers. Three RCTs investigated the therapeutic effects of acupuncture on histamine-induced itch, with stimulation mainly at acupuncture point LI11. These studies found a point-specific effect compared to sham-point stimulation in the same dermatome. Depth of insertion varied between the studies from superficial insertion to deep needling (Pfab et al., 2005; Belgrade et al., 1984; Lundeberg et al., 1987). A further RCT evaluated the effect of electrical ear acupuncture on histamine-iontophoresis induced itch, showing a point-specific effect of ear points (locus dolendi of the skin, reflection point of spinal cord dorsal root, thalamic point and sensitive spinal cord point of the corresponding body region) in comparison to placebo points elsewhere in the ear on alloknesis (Kesting et al., 2006).

## Nephrogenic itch

Pruritus is a common disabling problem in patients with advanced end-stage renal disease (Zucker et al., 2003) affecting about half of all hemodialysis and peritoneal dialysis patients. It has a great impact on patients' quality of life and is associated with increased mortality.

Acupuncture at acupuncture point LI11 for refractory uraemic pruritus in haemodialysis patients showed a significant reduction of itch scores compared to placebo acupuncture after a period of 4 weeks as well as 3 months (Che-Yi et al., 2005).

## Postoperative itch

Postoperative itching is a significant problem in postoperative care. Pruritus after surgery may be medication-induced (including intrathecal opioids) or secondary to a preexisting systemic disease (Waxler et al., 2005).

A recent review came to the conclusion that acupuncture is associated with reduced postoperative occurrence of nausea, dizziness, pruritus, sedation and urinary retention (Sun et al., 2008). Regarding the symptom of postoperative pruritus, pooled data from seven studies (Chen et al., 1998; Kim and Nam, 2006; Kotani et al., 2001; Lin et al., 2002; Sim et al., 2002; Usichenko et al., 2005; Wang et al., 1997) showed that pruritus occurred significantly less in the acupuncture group (23%) compared with the sham control group (34%) (RR: 0.75; 95% CI: 0.59, 0.96), with a number needed to treat (NNT) of 13 (NNT: average number of patients who need to be treated to prevent one additional bad outcome). The main acupuncture points used in these studies were LI4 and ST36. As pruritus was regarded as a side effect of opioid analgesics, the reduction in pruritus might be secondary to reduction in dose of opioids, rather than a primary effect.

## Atopic dermatitis

Atopic dermatitis (AD) is a non-contagious, chronically relapsing, inflammatory and pruritic skin disease, belonging to 'atopic diseases'. These diseases also include asthma and seasonal/environmental hypersensitivity reactions. Pruritus is a critical clinical component of AD (Ring, 2005; Williams et al., 1994; Bohme et al., 2000; Koblenzer, 1999) and leads to a serious impairment of quality of life of affected patients (Finlay, 2001; Yosipovitch et al., 2003; Behrendt et al., 2001; Stander et al., 2007).

A recent study found that acupuncture at acupuncture points LI11 and SP10 produced a significant reduction of clinically-relevant type I hypersensitivity itch sensation after verum acupuncture treatment compared to skin-penetrating sham-point treatment and no treatment in patients with AD (Pfab et al., 2010). Regarding the preventive influence, the specific acupuncture effect (difference between verum and sham-point acupuncture) diminished with regard to subjective itch sensation, whereas it increased the suppression of skin prick reactions.

A further study comparing electrical stimulation of acupuncture points LI11 and SP10 to cetirizine showed significant itch reduction after verum acupuncture or cetirizine treatment compared to sham acupuncture or placebo drug and no treatment in AD patients using a validated on-off itch model (Pfab et al., 2006, 2012). While preventive acupuncture (i.e. acupuncture applied before itch provocation) was similarly effective to cetirizine, abortive acupuncture (i.e. acupuncture applied concurrent to itch provocation) was significantly more effective than preventive acupuncture, sham acupuncture or cetirizine. In fact, abortive acupuncture was the only intervention to reduce itch below the clinically-relevant scratch urge threshold. Interestingly, preventive acupuncture was the only therapy to significantly reduce skin reactions (flare size). In this study, cognitive side effects (specifically regarding attention) were less pronounced for acupuncture compared to cetirizine.

Timing of acupuncture can be an important issue. In the case of allergic pruritus, acupuncture can be applied as preventative before exposure to an allergen or as symptomatic once the itch is present.

Salameh et al. investigated the effect of acupuncture treatment (individual selection of points) twice a week in combination with a Chinese herbal formula (*Dictamnus dasycarpus* (Faxinella; Bai Xiab Pi), *Lonicera japonica* (Lonicera flower), *Paeonia suffruticosa*, *Polygonum multiflorum*, *Rehmannia glutinosa* and *Sophora angustifolia*) 3 times daily for 12 weeks in an uncontrolled trial (Salameh et al., 2008). This treatment showed an improvement of itch intensity of nearly 50%.

Lee et al. compared the effect of acupressure using a 1.2 mm pellet fixed at the LI11 point, applying pressure for 3 min, 3 times per week for 4 weeks with standard care alone. Subjects given acupressure treatment showed an improvement in pruritus and lichenification (Lee et al., 2012). However, fully powered randomised controlled clinical trials are still lacking (Pfab et al., 2011).

Possible mechanisms for itch reduction by acupuncture in patients with AD include reduction of in vitro allergen-induced basophil activation and modulation of brain areas that are involved in itch processing such as the insula and putamen (Darsow et al., 2011; Pfab et al., 2008, 2011; Valet et al., 2008; Napadow et al., 2012). Furthermore, acupuncture may also modulate neurotransmitters and peripheral hormone levels related with atopic eczema and pruritus, such as beta-endorphin, ACTH and somatostatin (Dokukina et al., 1988; Iliev, 1998).

## Herpes zoster

This acute viral infection is characterised by inflammation of the sensory ganglia of certain spinal or cranial nerves and by pain and eruption of vesicles along the affected nerve path. Postherpetic itch is presumably caused by unprovoked firing of the peripheral and/or central neurons that mediate itch and occurs in neurons innervating skin left severely deafferented from shingles; pruritus, usually mild or moderate, commonly accompanies both acute zoster and postherpetic neuropathy (Oaklander, 2008; Oaklander et al., 2003).

## Cupping

Cupping therapy is a method mainly using horn, bamboo or glass cups on patients' skin by creating negative pressure inside the cups. In Traditional Chinese Medicine (TCM) this is used as an approach for diagnosis, treatment and prevention of disease. In a recent systematic review cupping was shown to exert a potential effect in the treatment of acute herpes zoster and prevention of postherpetic neuralgia (Cao et al., 2012); wet cupping (where a small incision is made in the skin before placement of cups) showed the best results. The evidence was inconclusive because of insufficient rigour.

## Acupuncture

Although acupuncture may ameliorate neuropathic pain and might therefore act as a therapeutic alternative, there are no randomised controlled studies to date. A large multicenter RCT is currently ongoing to investigate whether a 4 week semi-standardised acupuncture is superior to sham laser acupuncture and the anticonvulsive drug gabapentin in the treatment of pain and itch associated with herpes zoster (Fleckenstein et al., 2009).

## Combined therapy including acupuncture

In a non-blinded RCT an integrated complementary and alternative medicine (CAM) therapy with acupuncture, neural therapy (1% procaine injection as a local anaesthetic), cupping and bleeding, and TCM herbs compared to no therapy was associated with significantly reduced sub-acute and chronic postherpes zoster neuralgia pain within 3 weeks of initiating treatment; improvements persisted for up to 2 years (Hui et al., 2012).

## Sjögren syndrome/xerostomia

This systemic autoimmune disease in which immune cells attack and destroy the exocrine glands generally shows mouth and eye dryness as main symptoms.

Several experimental as well as clinical studies investigating the effect of acupuncture have been carried out pointing to a specific effect of acupuncture for up to 3 years duration (Deng et al., 2008; Garcia et al., 2009; Lu, 2005; Pinkowish, 2009; Jedel, 2005; Fox, 2004; Dawidson et al., 1997, 1998a,b, 1999; List et al., 1998). The effect may be due to increased levels of vasoactive intestinal polypeptid (VIP) and calcitonin-gene-related peptide (CGRP). Please refer to the palliative care Chapter 34 for more detailed information.

## Raynaud's phenomenon

This condition of the digital arteries causes the vessels to undergo spasm under conditions of cold or stress resulting in poor circulation and discoloration in the fingers, toes and uncommonly nose and ears. Primary Raynaud's phenomenon (RP) is idiopathic, not associated with other pathologies; secondary Raynaud's phenomenon appears in patients whose symptoms are secondary to pathology such as scleroderma, systemic lupus erythematoses or connective tissue diseases (Burgdorf and Braun-Falco, 2009).

A recent meta-analysis showed inconclusive evidence from two trials of acupuncture in RP (Malenfant et al., 2009).

Appiah et al., evaluated the effects of seven standardised acupuncture treatments compared to wait-list in 33 patients with primary RP showing a significant decrease in the frequency of attacks and duration of the capillary flowstop reaction (Appiah et al., 1997).

Schlager et al., evaluated the effect of auricular EA in 26 patients with idiopathic RP in a non-blinded study with no control group showing a reduction of symptoms in terms of frequency and severity of attacks but no influence on skin perfusion and skin temperature (Schlager et al., 2011).

Hahn et al., investigated the effect of acupuncture in a double blind, sham-controlled, randomised trial in patients with secondary RP. The study was performed during the winter season by licenced acupuncturists treating weekly for 8 weeks (points chosen for the verum group: LI4, TE5, ST36, PC6, GV20, EX28). An improvement was detected in both groups (verum and sham) but no point-specific effect of acupuncture (Hahn et al., 2004).

Maeda et al., described 24 patients with secondary RP due to progressive systemic sclerosis: Low-frequency EA showed reduction of vasoconstricting plasma-endothelin-level and an increase in peripheral blood perfusion (Maeda et al., 1998).

## Psoriasis

Psoriasis is a non-contagious inflammatory skin condition that affects the life cycle of skin cells causing cells to build up rapidly on the surface of the skin to form thick silvery scales and itchy, dry, red patches that are sometimes painful (Burgdorf and Braun-Falco, 2009).

A typical phenomenon in psoriasis is the Koebner phenomenon or 'isomorphic response,' which refers to skin lesions appearing on lines of trauma. Acupuncture can be such a traumatic factor triggering psoriasis flares (Wu and Caperton, 2013).

Jerner et al. compared EA (through needles placed intramuscularly plus ear acupuncture) to sham (minimal) acupuncture over a period of 10 weeks showing a slightly better effect in the sham group (Jerner et al., 1997).

Acupuncture does not seem promising in this genetically determined disease that can be triggered by physical skin stress.

## Other skin conditions

Patients are often very aware of their skin conditions, so those with chronic conditions are likely to continue trying different treatments, and ultimately acupuncture. There is no evidence that acupuncture has any therapeutic effect on acne vulgaris, alopecia or baldness, nor that it has any lasting cosmetic benefit. Possible mechanisms have been described that may be relevant in some of these conditions, but this is insufficient to recommend acupuncture.

## Skin side effects of acupuncture

Side effects of acupuncture are rare (MacPherson et al., 2001). Besides common and well known symptoms of local erythema, hematoma or irritation at needle insertion site occasionally wheal formation can be witnessed. Case reports have described local granuloma formation (Alani and Busam, 2001), pseudolymphoma (Kim et al., 2002), dermatitis (Koizumi et al., 1989), panniculitis (Lee et al., 1995), argyria (Rackoff et al., 2007; Kakurai et al., 2003; Takeishi et al., 2002; Suzuki et al., 1993; Matsumura et al., 1992), infections (Ara et al., 2003; Ryu et al., 2005; Wagner, 1990) after acupuncture as well as scar formation after moxibustion (Hung and Mines, 1991; Pigatto and Guzzi, 2004).

## Concluding comments

In summary, acupuncture has shown promise in postoperative, nephrogenic, atopic dermatitis and histamine-induced itch. Furthermore cupping seems a promising option in herpes zoster. Little evidence exists for mouth dryness in Sjögren syndrome and idiopathic Raynaud's phenomenon. The evidence regarding psoriasis does not seem promising. Large RCTs are needed for acupuncture in the field of dermatology.

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# Acupuncture in gynaecology and infertility

E. Stener-Victorin

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## Introduction

The use of acupuncture in gynaecology and infertility is widespread although the evidence is not of highest level. In this chapter the pathophysiology of common gynaecological and reproductive dysfunctions is discussed and a summary of current evidence is presented which for most conditions indicates that acupuncture is a suitable alternative or complement to pharmacological treatment, with few adverse side effects.

## Dysmenorrhoea and endometriosis

Dysmenorrhoea affects approximately 25% of women of reproductive age, but is even more common in young women in their late teenage years. The main characteristic of dysmenorrhoea is painful menstruations that interfere greatly with daily activities as well as health-related quality of life. The quality of the pain may vary but is usually described as sharp or dull, throbbing, and nauseating and is associated with cramps in the lower abdomen and sometimes in the back. The cramps are referred from uterine contractions which are stronger and of greater frequency during menstruation as compared with the rest of the menstrual cycle. Many women also experience premenstrual dull aching in the lower abdomen, as well as irritability and symptoms of depression. The diagnosis is usually based on a medical history and the timing of pain during menstruation.

Dysmenorrhoea is classified as primary or secondary: in primary there is no underlying condition and secondary is associated with an existing condition. The most common cause of secondary dysmenorrhoea is endometriosis as described later.

The cause of dysmenorrhoea is not completely understood. During menstruation prostaglandin  $F_{2\alpha}$  is produced and released from the endometrium which causes uterine contractions of the myometrium (Lethaby et al., 2007). Uterine contractions constrict the endometrial blood flow which in turn results in a temporary lack of oxygen which, in part, may contribute to the typical cramp-like menstruation pain.

Endometriosis affects approximately 10% of women of reproductive age. The main characteristic of endometriosis is constant abdominal pain during the menstrual cycle with increased intensity during menstruation. Often endometriosis is associated with symptoms of depression. Endometriosis is defined as abnormal presence of endometrial tissue outside the uterus in the abdominal/pelvic cavity (Farquhar, 2007). The diagnosis is made by the combination of tissue biopsies identifying endometrial cells and stroma outside the uterus and an appropriate medical history.

As for dysmenorrhoea, the cause of endometriosis is not completely understood. The ectopic endometrial implants initiate an inflammatory response by recruitment of immune cells and macrophages and by activation of glial cells (for review see Lundeberg and Lund, 2008). In addition to an inflammatory response, sex steroids seem to play a major role by enhancing the pain response in endometriosis patients. Of special note is that endometriosis has been demonstrated to be oestrogen dependent and that estrogens have the potential to enhance the production and secretion of prostaglandin and nerve growth factor in uterus. This may in turn promote sensitisation and nerve sprouting in the affected cells (Shi et al., 2006).

## Treatment of dysmenorrhoea and endometriosis

There is limited evidence on treatment for both dysmenorrhoea and endometriosis. First-line treatment of dysmenorrhoea includes analgesics; nonsteroidal anti-inflammatory drugs; paracetamol; aspirin; and paracetamol-opiate combination analgesics (Proctor and Farquhar, 2006). For endometriosis, evidence supports first-line treatment with combined oral contraceptives, progestogens, danazol and gonadotrophin releasing hormone agonists (Farquhar, 2004). Laparoscopic excision of deep and nodular ectopic endometriotic tissue has been shown to result in pain relief. In addition, antidepressants have neuromodulatory and pain-relieving properties although there is limited data on the efficacy of such pharmacological treatment for relief of symptoms related to dysmenorrhoea and endometriosis.

Non-pharmacological treatment includes exercise which decreases ratings of menstrual distress (Israel et al., 1985); heat pad; relaxation treatment; transcutaneous electrical nerve stimulation; as well as multidisciplinary approach including lifestyle changes and behavioural therapy, although the latter does not decrease pain scores, but improves daily activities and non-pain symptoms.

## EVIDENCE ON ACUPUNCTURE FOR DYSMENORRHOEA

Acupuncture has been demonstrated to improve symptoms, and the Cochrane review from 2011 states that there exists some evidence for the use of acupuncture in managing period pain (Smith et al., 2011b). However, due to the small number of studies and study participants it is also concluded that the findings should be interpreted with caution. Importantly, no significant adverse effects were identified in this review. The results two most well conducted trials presented will now be summarised (Smith et al., 2011a; Witt et al., 2008).

The largest randomised acupuncture study in women with dysmenorrhoea investigates the clinical effectiveness and cost-effectiveness of acupuncture in this condition (Witt et al., 2008). In total 649 women were included and randomised to acupuncture, 15 treatments over 3 months ( $n = 104$ ), or to a control group receiving no acupuncture ( $n = 104$ ). In addition, patients who fulfilled the inclusion criteria but declined participation were included in a third arm and also received immediate acupuncture treatment. All participants were allowed to receive usual medical care. The number of needles and acupuncture points used were chosen at the physician's discretion. Only needle acupuncture with manual stimulation was allowed.

In the primary analyses, the average pain intensity at 3 months was lower in the acupuncture group, and the proportion of responders was 63.4% in the acupuncture group as compared to 24.0% in the control group. All subscales, except general health perception, in the health-related quality of life measure SF36 improved more in the acupuncture group compared to the controls. At 6 months when the control group had received acupuncture, there were no longer any differences between the groups. Among the randomised patients, acupuncture was associated with lower overall and diagnosis-specific costs. The authors conclude that acupuncture in addition to routine care results in clinically relevant benefit and is a cost-effective treatment for women with dysmenorrhoea (Witt et al., 2008).

### Clinical points

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Acupuncture is effective for treating dysmenorrhoea, but it is uncertain whether this is a specific effect.

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Another recent trial investigated the effectiveness of acupuncture to reduce the severity and intensity of primary dysmenorrhoea in 92 women (Smith et al., 2011a). Directly after the 3-month treatment period, although there was a reduction in pain rating in the acupuncture group, there were no differences between the acupuncture and the control group which received sham acupuncture with non-penetrating needles with the same timing and duration as in the active acupuncture group.

Sham points were non-acupuncture points, and placebo needles with blunted tip (non-penetrating) were placed 2–4 cm away from classical acupuncture points. However, at the follow-up 3 months after the last treatment, the acupuncture group demonstrated a reduction in menstrual pain and reduced need for additional analgesia as compared with the control group (Smith et al., 2011a). In addition, acupuncture improved women's mood symptoms during the treatment period.

### Clinical approach

In a typical protocol, acupuncture was given weekly for 3 weeks followed by a week of no treatment during the week of expected menses for three menstrual cycles (Smith et al., 2011a). The acupuncture protocol was semifixed and was given according to TCM diagnoses and standardised to each patient. A minimum of seven points were used at each treatment. Acupuncture needles ( $0.2 \times 30 \text{ mm}^2$ ) were inserted to a depth of  $\leq 2 \text{ cm}$  and stimulated manually when inserted and after 15 min of each 30 min treatment session. Importantly, most of the points given below are located in the same innervation area as uterus supporting the importance of selecting segmental points in the treatment of dysmenorrhoea (Table 32.1).

**TABLE 32.1 ■ Acupuncture points used for dysmenorrhoea in the Smith et al. study using traditional not Western Medical approach (Smith et al., 2011a)**

Primary acupuncture points used in all patients at every treatment	SP4, 6, 8, ST29, CV3 and BL23
<i>Example of diagnostic patterns</i>	
Qi and blood stagnation	SP4, 6, 8, 10, LR3, CV3, 6, BL32, LI4
Qi and blood deficiency	SP6, 8, ST36, CV6, 34, BL17, 20, 32
Stagnation of cold	SP6, ST36, KI6, CV3, 4, 6, GV4, BL23, LU7
Accumulation of damp heat	SP6, 9, LR2, ST40, 28, 29, BL22, 32, GB34, LI11
Kidney and Liver deficiency	SP6, KI3, ST36, CV4, 6, BL17, 18, 23

## EVIDENCE ON ACUPUNCTURE FOR ENDOMETRIOSIS

The Cochrane review on acupuncture for pain in endometriosis concludes that there exists limited evidence of acupuncture for pain in endometriosis (Zhu et al., 2011). One study evaluated the efficacy of Japanese acupuncture - which involves superficial insertion of thin needles with mild manipulation - in 18 adolescents and young women. All participants received 16 treatments, twice a week during eight consecutive weeks. Treatments were individualised according to patients' diagnostic symptoms. Treatment protocol included needling of 8–12 points (points not stated), moxibustion on back shu points and in the sacral region, and electrical stimulation of auricular points. Sham was designed to mimic active acupuncture while being minimally active. They found a significant improvement in pain rating and health-related quality of life in the verum-acupuncture group as compared to the control group, which persisted 6 months after the last treatment (Wayne et al., 2008).

In another trial, 101 women with endometriosis (stage II–IV, ASRM 1996) (Vercellini et al., 1996) diagnosed by laparoscopy and a pain intensity  $\geq 50$  according to a visual analogue scale were randomised into one of two groups; Group 1 ( $n=47$ ) received verum-acupuncture and Group 2 ( $n=54$ ) received nonspecific acupuncture (Rubi-Klein et al., 2010). The course of ten treatments was followed by an observation period of at least two menstrual cycles. Thereafter a second set of treatments was given according to a crossover design (Group 1 received the Group 2 protocol and vice versa).

The authors report that verum-acupuncture significantly reduced the pain intensity and improved quality of life after the first and second sets of 10 treatments each. However, they do not report the primary analysis which is given as difference in VAS pain ratings between verum-acupuncture and sham. Further it is reported that Group 2 decreased their pain intensity after the second set of treatment, but again they fail to report the primary outcome measures.

### Clinical approach

Based on the trial by Rubi-Klein with the largest study population and well described protocol, below the protocol is described in detail. Each participant received 10 acupuncture treatments twice a week during 5 weeks.

The active acupuncture group received up to 15 points whereas the control received only eight points (Table 32.2). Needles in group I were stimulated manually and/or by moxa, whereas needles in Group 2 were placed subcutaneously without further stimulation.

Limited evidence suggests acupuncture may relieve symptoms and improve in health-related quality of life for adolescents and women with dysmenorrhoea and endometriosis. No negative side effects have been reported.

TABLE 32.2 ■ Acupuncture protocol for endometriosis

	Points
<i>Group 1 – active acupuncture</i>	
Fixed points	BL32, ST29, ST36, CV3 and SP6
Additional points (maximum three according to TCM diagnosis)	LI3, LI8, SP9, SP10 or KI10
<i>Group 2 – sham acupuncture</i>	
Designed not to correlate to endometriosis	SI9, GB31, LU1 and ST8

## Vulvodynia

Vulvodynia (formerly vulvar vestibulitis syndrome) means ‘pain in the vulva’ and includes clinical features such as continuous pain in the major part of the vulvar area, whereas others suffer from more localised pain, usually provoked by vaginal intercourse or tampon use (Bohm-Starke, 2010). The symptoms impair the patients’ sexual function and psychological well-being. Research on the pathophysiology of vestibulitis suggests abnormalities in three interdependent systems: vestibular mucosa with an initial inflammatory response which may result in peripheral and central pain sensitisation, dysfunction of the pelvic floor muscles, and dysfunctional central nervous system pain regulatory pathways.

Cognitive-behavioural therapy is among the most popular first-line interventions (Desrochers et al., 2010) although surgery is the treatment proven to be most effective (Tommola et al., 2010). In addition, as in the treatment of dysmenorrhoea and endometriosis, antidepressant medication may cause pain relief and improve mental health.

## EVIDENCE ON ACUPUNCTURE

There are three uncontrolled trials (Curran et al., 2010; Danielsson et al., 2001; Powell and Wojnarowska, 1999) investigating the pain relieving effect of acupuncture in women with vulvodynia.

In the study by Powell et al., 12 women with vulvodynia were treated with acupuncture (Powell and Wojnarowska, 1999). All had experienced severe distress and impairment of sexual function and usual treatments had failed. The patients attended weekly for 5 weeks. Half had treatment for the first 5 weeks, the other half for the second 5 weeks. No information is given about stimulation and duration of each treatment. The results were impressive, as for many uncontrolled trials, with two women improved so much that they declared themselves ‘cured.’ In addition, symptoms were improved in three, and four felt slightly better, while the rest did not respond.

In the second study, acupuncture was given 10 times, at an interval of 1–2 treatments a week in 14 women with vulvodynia (Danielsson et al., 2001). Four local and two distal acupuncture points were used each time, and when deemed possible or necessary by the acupuncturist, another 1–3 local and 1–2 two distal points were also applied (Table 32.3). The needles were inserted into the acupuncture points into the muscles until *de qi* was felt and stimulated 1–3 times during each treatment which lasted for 30–45 min. Health-related quality of life was improved after treatment, and the effect lasted at the 3 months follow-up.

In the third study, 10 acupuncture treatments were given during 5 weeks. The selection of acupuncture points was based on TCM diagnosis and approximately 10–20 needles were inserted at each treatment (see Table 32.3). Each treatment lasted for 20–25 min but no information is given about the stimulation. A decrease in pain with manual genital stimulation and improvement in helplessness was observed. Although a nonsignificant change, there was an improvement in sexual desire and the ability to have intercourse.

TABLE 32.3 ■ Acupuncture protocols used in the treatment of vulvodynia

Study	Points
Powell and Wojnarowska (1999)	SP6, 9, LR3 and LI4
Danielsson et al. (2001)	CV3, 4, 5, 6, GV3, BL31, 33, SP9, ST36, LR8 and KI3
Curran et al. (2010)	CV3, BL32, 33, 40, LU7, KI6, PC6, SP4, 6, 8, 10, ST30, 36, LR2, 3, 5, GB34, 41

Uncontrolled trials indicate that acupuncture may provide useful relief of symptoms associated with vulvodynia. No adverse effects were observed. Other pharmacological and non-pharmacological treatment have limited evidence. Therefore acupuncture may be a reasonable alternative and/or complementary treatment.

## Pelvic girdle pain during pregnancy

Pelvic girdle pain refers to pregnancy-related pain in the lumbosacral, sacroiliac and symphysis pubis joints. There is no consensus on the incidence although it is estimated to be 20% of which approximately 5–8% have severe disabling pain (Kanakaris et al., 2011). Previous back pain and pelvic girdle pain are known risk factors, as well as strenuous work. The cause is multifactorial and most often no obvious explanation can be found. It may be due to a combination of factors, such as asymmetrical movement and abnormal biomechanics of the pelvic girdle, and hormonally induced pain in the pelvic girdle. The diagnosis is based on symptoms and clinical examination, and the most reliable diagnostic test is the positive posterior pelvic pain provocation test (Elden et al., 2005). It is of importance to differentiate between pelvic pain and low back pain since the advice and exercise differs.

Treatment of pelvic girdle pain during pregnancy is limited because of the potential hazards to the foetus. Pelvic belt, home exercise program, education, water gymnastics, individualised stabilising exercise and acupuncture have been identified as being beneficial for reduction of pain and sick leave (Kanakaris et al., 2011).

## EVIDENCE ON ACUPUNCTURE

Acupuncture as an adjunct to standard treatment has been demonstrated to be the method of choice for patients with pelvic girdle pain during pregnancy and was superior to stabilising, individualised exercise (Elden et al., 2005).

A total of 386 pregnant women with pelvic girdle pain were randomised to 6 weeks of standard treatment, standard treatment plus acupuncture or standard treatment plus stabilising exercise. Standard treatment included advice about activities and information on the condition and anatomy of the back and pelvis, as well as home exercise programme. The acupuncture group received a 30 min acupuncture treatment twice a week for 6 weeks, in total 12 treatments. At each treatment, a total of 10 points in the painful area were selected individually after palpation, and seven distal, fixed points in the arm/hand and leg/feet (Table 32.4). Needles were manually stimulated every 10 min. This treatment has to be considered as relatively strong. Notably, no negative side effects were reported (Elden et al., 2008c). Minor adverse events were reported by the mother but had no adverse influence on the pregnancy, delivery or the foetus/neonate. Importantly, in the same study, they followed the women 12 weeks postpartum with the aim of describing regression of pelvic pain after delivery (Elden et al., 2008b). Three weeks after delivery, three-quarters of all women were pain free, and 12 weeks after delivery 99% were free from pelvic girdle pain. This is an important message to the pregnant woman that, irrespective of

TABLE 32.4 ■ Acupuncture protocols used in the treatment of pelvic girdle pain during pregnancy

References	Points
Elden et al. (2005, 2008a)	Local points: BL26, 32, 33, 54, KI11, EX21, GB30, SP12 Distal points – Always used: GV20, LI4, ST36, BL60
Lund et al. (2006)	Local points: BL27, 28, 29, 31, 32, 54, KI11, CV3 Distal points: SP6, LR2, LI4

treatment during pregnancy, her pelvic girdle pain will most likely resolve within 12 weeks after delivery (Elden et al., 2008b).

In a follow-up study ( $n=115$ ) the same group investigated whether acupuncture with needles placed in muscle tissue has a greater treatment effect than non-penetrating sham acupuncture in women with pelvic girdle pain during pregnancy (Elden et al., 2008a). The same acupuncture protocol was used as described earlier. There was no difference in reduction in pain between the two groups. Women in the group with penetrating needles were more likely to return to work and had a better ability to perform daily activities compared to women in the non-penetrating sham acupuncture group. This study supports other evidence than non-penetrating sham acupuncture is not an inert sham procedure as discussed in Chapter 17 (Clinical Trials).

Clinical points

Acupuncture reduces girdle pain in pregnancy though this may not be a specific effect.

There is one smaller study ( $n=47$ ) with a similar treatment protocol demonstrating that acupuncture ameliorates pelvic girdle pain during pregnancy to the same extent as superficial needling (Lund et al., 2006). Ten treatments over 5 weeks were given and at each treatment 10 needles were placed and stimulated five times during 30 min (see Table 32.4). This study demonstrated that both acupuncture with needle insertion into the muscle and superficial needle insertion decrease pain intensity and improve daily activities, although no group differences was observed.

There is good evidence that acupuncture decreases pelvic girdle pain during pregnancy without any negative side effects, though it may not be a specific effect. Stabilising exercise was also demonstrated to be effective, and one may propose that the combination of these two interventions would result in the most beneficial effects.

Polycystic ovary syndrome

Polycystic ovary syndrome (PCOS), also called the female metabolic syndrome, is characterised by three features: clinical or biochemical hyperandrogenism, oligo- or amenorrhoea and polycystic ovaries (PCOs) with or without increased ovarian volume (PCOS, 2004; Azziz et al., 2009; Norman et al., 2007). Hyperandrogenism is the most constant and prominent feature, manifested by hirsutism, persistent acne and biochemical abnormalities (Azziz et al., 2009), with elevated levels of circulating androgens and oestrogens (Stener-Victorin et al., 2010). The metabolic abnormalities include overweight/obesity, hyperinsulinaemia, insulin resistance and progression to type 2 diabetes, and dyslipidaemia, which may contribute to hyperandrogenism in women with PCOS (Norman et al., 2007). High circulating levels of androgens in women with PCOS is also associated with high sympathetic nerve activity (Sverrisdottir et al., 2008). In addition to the endocrine and metabolic features, health-related quality of life and psychological well-being are

lower in women with PCOS (Barnard et al., 2007; Coffey et al., 2006; Elsenbruch et al., 2003), and symptoms of depression and anxiety are more prevalent (Benson et al., 2009; Elsenbruch et al., 2006; Himelein and Thatcher, 2006; Hollinrake et al., 2007; Jedel et al., 2010; Kerchner et al., 2009; Mansson et al., 2008).

The aetiology and pathogenesis of PCOS remains unclear and poorly understood (Azziz et al., 2009; Norman et al., 2007). The heterogeneity of the syndrome may reflect multiple underlying mechanisms. Androgens and insulin are two key endocrine mediators, and there is a strong association between hyperinsulinaemia and hyperandrogenism, but the mechanisms behind their relationship and their associations with PCOS are not fully understood (Schuring et al., 2008). Whether hyperandrogenism results from the hyperinsulinaemia of insulin resistance or vice versa is still not clear. Obesity is more common in PCOS and may amplify its effects. The most common theories to explain the pathogenesis of PCOS are neuroendocrine or genetic defects, impairments in ovarian steroidogenesis or adrenal androgen production, insulin resistance with compensatory hyperinsulinaemia and increased sympathetic activity.

Many women with PCOS require prolonged treatment. Since the aetiology of the syndrome is unclear, the treatment is most often symptom oriented and focused on reducing clinical and biochemical hyperandrogenism, restoring menstrual cycles, inducing ovulation and improving reproductive outcome. Treatment should also address metabolic disturbances including hyperinsulinaemia, insulin resistance and obesity, which worsen many of the typical PCOS-related symptoms and affect long-term metabolic morbidity.

## EVIDENCE ON ACUPUNCTURE IN THE TREATMENT OF IRREGULAR CYCLES IN PCOS

In uncontrolled trials, repeated acupuncture treatments decreased total testosterone and other sex-steroid levels, reduced luteinizing hormone (LH)/follicle-stimulating hormone (FSH) ratio, and improved menstrual frequency without negative side effects (Chen and Yu, 1991; Gerhard and Postneek, 1992; Stener-Victorin et al., 2000). In a three-arm randomised controlled trial (RCT), fourteen low-frequency electroacupuncture (EA) treatments (combination of electrical and manual stimulation) over 16 weeks, and 16 weeks of physical exercise, improved menstrual bleeding pattern and decreased high levels of circulating androgens compared with no intervention in women with PCOS (Jedel et al., 2011). Acupuncture was superior to physical exercise when compared directly after the treatment but did not differ from the exercise group at 4-month follow-up.

In a quasi-randomised study, daily abdominal acupuncture for 6 months improved menstrual frequency and decreased circulating testosterone more effectively than metformin over 6 months (Lai et al., 2010). In another RCT, a course of 12 treatments of true acupuncture was compared with sham acupuncture for 8 weeks, and they found similar ovulation frequency and improvement in LH/FSH ratio in both groups of women with PCOS (Pastore et al., 2011). Thus, they were unable to demonstrate differences between true and sham acupuncture and they did not include a nonintervention group. These results are in line with previous studies on different pain conditions and nausea caused by chemotherapy, demonstrating that true acupuncture is not more effective than sham acupuncture, although all these trials found a significant effect when compared with a nonintervention group (Enblom et al., 2011). These results indicate that sham acupuncture is not an inert method and highlight methodological difficulties in the design of acupuncture trials.

In another trial, the efficacy of low-frequency EA in combination with manual stimulation, 30 min twice a week for 10–13 weeks (more intensive treatments than in the previous trials) in total 20–26 treatments was compared with equal time in meetings with a therapist (to control for attention and expectations) for ovulation induction in women with PCOS (Johansson et al., 2013). Women receiving acupuncture treatment displayed higher ovulation frequency compared

**TABLE 32.5 ■ Acupuncture protocols in the treatment of polycystic ovary syndrome for ovulation induction**

References	Points
Jedel et al. (2011)	Local points: CV3, 6 – EA; ST29 bilateral – EA Distal points: SP6, 9 bilateral – EA; LI4 or PC6 bilateral – manual
Johansson et al. (2013)	Alternated between two protocols every other treatment Protocol 1: Local points: CV3, 6 – EA; ST 29 bilateral – EA Distal points: SP6, 9 – EA; LI4 bilateral, GV20 – manual Protocol 2: Local points: ST25, 29 – EA; CV3, 6 – manual Distal points: SP6, LR3 bilateral – EA, PC6 bilateral, GV20 – manual

In both trials local points and some distal points acupuncture points are selected in somatic segments innervating the ovaries.  
EA – electroacupuncture, 2 Hz; manual – *de qi* 3–4 times during 30 min.

with women meeting a therapist for an equal amount of time (Johansson et al., 2013). Also the ovarian and adrenal sex-steroid levels were reduced with no effect on LH secretion indicating that this regulation occurs at ovarian level. These results indicate that more frequent treatment results in more pronounced effects (Table 32.5).

**Metabolic abnormalities**

Reviews support the hypothesis that acupuncture has beneficial effects on obesity and insulin sensitivity in T2D with no negative side effects (Cho et al., 2009; Liang and Koya, 2010). The studies included in these reviews, however, were underpowered and of poor methodological quality. We performed secondary analyses on metabolic variables in our RCT (Jedel et al., 2011) and found no effect of acupuncture on insulin sensitivity (Stener-Victorin et al., 2012). However, in our experimental studies on dihydrotestosterone-induced PCOS rats that exhibit PCOs, irregular cycles, obesity and insulin resistance (Feng et al., 2009; Mannerås et al., 2007; van Houten et al., 2012), we found that more frequent acupuncture treatments than we used in our RCT (Fig. 2A) or 4–5 weeks of voluntary exercise ameliorated insulin resistance (Johansson et al., 2010; Manneras et al., 2008). This effect may involve regulation of adipose and skeletal muscle tissue signalling pathways because acupuncture and exercise each partly restore divergent gene and protein expression associated with insulin resistance, obesity and inflammation (Johansson et al., 2010; Manneras et al., 2008).

**Mental health**

Secondary analyses of the previously published RCT indicate that acupuncture and exercise may improve symptoms of anxiety and health-related quality of life, although the effect was modest (Stener-Victorin et al., 2013). There is a great need of further research within this area.

The evidence indicates that acupuncture induces more regular menstrual cycles and ovulation in women with PCOS, and may serve as an alternative or complement to standard care.

**Acupuncture and in vitro fertilisation**

Approximately 7–17% of all couples have difficulty conceiving at some point in their reproductive life (Evers, 2002; Oakley et al., 2008; Stephen and Chandra, 1998). One of the most commonly used treatment options is in vitro fertilisation (IVF). In addition to first-line conventional therapy,

many infertile couples utilise complementary and alternative therapies (de Lacey et al., 2009). Infertile women attempt many things in the hopes of overcoming their infertility, and acupuncture is no exception.

## EVIDENCE ON ACUPUNCTURE 4 WEEKS PRIOR TO OOCYTE ASPIRATION

The first study in the area was uncontrolled and demonstrated that repeated low-frequency EA treatments twice a week during 4 weeks prior to oocyte retrieval and embryo transfer (ET) decrease a high pulsatility index (PI) in the uterine arteries (Stener-Victorin et al., 1996) and thus improve endometrial circulation. This finding was recently confirmed demonstrating that four treatments prior oocyte retrieval decrease PI index (Ho et al., 2009). None of these studies had the power to investigate pregnancy outcome. However, both studies indicate that acupuncture increases uterine artery blood flow which is one of many factors important for successful implantation (Steer et al., 1995).

## PAIN RELIEF DURING OOCYTE ASPIRATION

Next acupuncture was tested for pain relief during oocyte retrieval (Stener-Victorin et al., 1996). Acupuncture was demonstrated to induce similar pain relief as fast acting opiate (alfentanil) (Stener-Victorin et al., 1996, 2003). Although the initial trial demonstrated an increased pregnancy rate, when repeated with larger number of patients and adequate power calculation, there were no differences in IVF outcome (Gejervall et al., 2005; Humaidan and Stener-Victorin, 2004; Stener-Victorin et al., 2003). Auricular acupuncture with electrical stimulation in addition to conventional analgesia (patient controlled analgesia with remifentanyl) during oocyte retrieval induced a significant reduction in pain ratings and improved well-being and also reduced opioid requirement compared to no acupuncture and auricular acupuncture without electrical stimulation (Sator-Katzenschlager et al., 2006).

Acupuncture may be used as a complement to standard analgesia to reduce the dose of fast acting opiates, decrease subjective pain and increase well-being during and after oocyte retrieval.

## EVIDENCE FOR ACUPUNCTURE DURING ET

The first RCT elucidating the efficacy of acupuncture given before and after ET suggested that acupuncture increases the pregnancy rate (Paulus et al., 2002). However, the power calculation was based on the Stener-Victorin study (Stener-Victorin et al., 1999) which clearly states that the sample size in that study was not large enough to elucidate whether acupuncture increases pregnancy outcome or not. Since then, a large number of RCTs and several systematic reviews and meta-analyses of RCTs have investigated whether adding acupuncture to the ET procedure increases the IVF success rate. These meta-analyses have had conflicting findings, and the RCTs included had heterogeneous methods and results.

In total, at least 11 RCTs have investigated the efficacy of acupuncture during ET. Three of them found a statistically significant benefit of acupuncture relative to control (Dieterle et al., 2006; Paulus et al., 2002; Westergaard et al., 2006), six found no statistically significant difference (Andersen et al., 2010; Benson et al., 2006; Domar et al., 2009; Moy et al., 2011; Paulus et al., 2003; Smith et al., 2006), while two found a statistically significant benefit of the control relative to acupuncture (Craig et al., 2007; So et al., 2009). The major question is what might explain the heterogeneity in these results in the RCTs? One explanation may simply be the number of patients included. Another may be the drawbacks of using the sham acupuncture control that may

Table 32.6 ■ Acupuncture protocols used (A) for oocyte aspiration; and (B) during ET

References	Points
<i>Oocyte Retrieval</i>	
Stener-Victorin et al. (1999), Stener-Victorin et al. (2003) and Gejervall et al. (2005)	Local points: ST29 – KI11 – EA 80Hz Distal points: LI4 – 10 – EA 2Hz, ST36, bilateral – manual, GV20 – manual
<i>Embryo transfer</i>	
Paulus et al. (2002)	Points before ET: GV20, ST29, SP8, PC6 and LR3 Points after ET: ST36, SP6, SP10 and LI4 In addition, auricular acupuncture at the following points, no stimulation: Shenmen, Zhigong, Neifenmi, Naodian

EA – electroacupuncture, 2Hz; manual – *de qi* 3–4 times during 30 min.

have its own effects on the IVF outcome (So et al., 2009, 2010). Further, lower, but not higher, baseline pregnancy rates predict a higher pregnancy rate after acupuncture, and this could not be explained by any confounding variables evaluated (Manheimer et al., 2013).

Interestingly, one trial applied the combination of the Stener-Victorin et al. protocol (Stener-Victorin et al., 1996) including treatment 4 weeks prior oocyte retrieval/ET with the Paulus et al. protocol (Paulus et al., 2002) including treatment before and after ET. They received nine treatments before oocyte retrieval with one treatment within 24 h before and one treatment within 1 h after the ET (Magarelli et al., 2009). The main outcome was a beneficial regulation of cortisol and prolactin in the acupuncture group with a trend toward more normal fertile cycle dynamics. They also applied the combination of these protocols on patients with poor response and found an increased pregnancy rate (Magarelli and Cridenda, 2004).

From a physiological point of view it is more reasonable that pretreatment prior to oocyte retrieval and ET will result in increased pregnancy rate since it has the potential to increase uterine artery blood flow and regulate the hormonal milieu (Table 32.6).

Acupuncture 3–4 weeks prior to oocyte retrieval and ET increases uterine artery blood flow. Whether acupuncture before and after ET improves IVF outcome remains uncertain. Further studies are necessary.

## Acupuncture for hot flushes in women with breast cancer

Acupuncture has been compared with applied relaxation and both treatments improved psychological well-being and vasomotor symptoms in women with breast cancer (Nedstrand et al., 2006). Also, acupuncture was found to be as effective as venlafaxine but with fewer side effects (Walker et al., 2010). Filshie et al. report an approach for long-term treatment in women suffering from vasomotor symptoms due to breast cancer therapy (Filshie et al., 2005). Initially, six weekly acupuncture treatments were given with needling of LI4, TE5, LR3 and SP6 and two upper sternal points. Needles were inserted approximately 1 cm and the sternal needles were inserted to touch the periosteum on the midline of the upper manubrium (Filshie et al., 2005). Needles were left in place 10 min without stimulation. If patients tolerated the treatment, they were instructed how to perform self-acupuncture using semipermanent needles or conventional needles at SP6, weekly for up to 6 years. In this retrospective study including 194 cancer patients providing records, acupuncture including self-acupuncture was associated with long-term relief of vasomotor symptoms (Filshie et al., 2005).

## CLINICAL APPROACH

Most studies stimulate needles manually and their point selection is based on TCM diagnosis. Therefore, no fixed protocols can be recommended. Interestingly, the points SP6, LR3, KI6, 7, CV4, LI4, LU7 and HT6 repeatedly occur independent of TCM diagnosis and may be recommended in the treatment of hot flushes. Stimulation is often manual manipulation of the needles. If electrical stimulation is used, its low-frequency EA.

Acupuncture improves vasomotor symptoms and well-being when compared with usual care in postmenopausal women as well as in cancer patients, though the effect of the needles themselves is uncertain.

## Concluding comments

Acupuncture is widely used in gynaecological disorders and particularly in infertility. It is effective for dysmenorrhoea and endometriosis, and pelvic girdle pain during pregnancy, though it is not clear whether this is a specific effect. Some early studies suggest it may be of benefit for vulvodynia.

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# Acupuncture in obstetrics

C.A. Smith

## CHAPTER OUTLINE

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## Introduction

The use of acupuncture in pregnancy is an emerging area of clinical practice. Over the last decade acupuncture has increasingly been used in maternity units in Western settings, and this has been mirrored by increasing referral patterns by maternity professionals particularly midwives (Adams et al., 2011a). Surveys indicate acupuncture is used throughout pregnancy, including the first trimester, to treat a wide range of conditions. Data from a cohort of women recruited to the Australian Longitudinal Study on Women's Health indicate 32.8% of pregnant women used complementary therapies during their pregnancy (Adams et al., 2011b), with 6% using acupuncture. Overall, women who used complementary therapies in this study experienced poorer health status and used these modalities to manage headaches or migraines (44%), back pain (39%), difficulties sleeping (29%) and severe tiredness (46%).

Comparatively little is known about how acupuncture is used in every day clinical practice with pregnant women. Textbooks describe the application of acupuncture to treat a wide range of complaints during pregnancy including morning sickness, carpal tunnel syndrome, headaches including migraines, pelvic pain, sciatica, indigestion, haemorrhoids and depression. It is also used for birth preparation, pain management in labour, retained placenta, and postpartum complaints including breast soreness and insufficient milk supply (Betts, 2006; West, 2000; Maciocia, 1998).

Frequent advice given to newly qualified practitioners may include avoiding working with pregnant women until gaining more clinical experience. General guidelines for the practice of acupuncture in pregnancy relate to needling techniques, and the application of moxibustion. Advice on needling includes using fewer needles during a treatment session than with non-pregnant patients, and using minimal needle stimulation (Betts, 2006), with the needle left in place for 15–20 min after eliciting *de qi*, without further needle stimulation.

## The safety of acupuncture use during pregnancy

In general acupuncture is considered to be a safe modality with the risk of minor side effects small (a risk of 1.3 per 1000 treatments) (Bensoussan et al., 2000). These side effects may include, nausea, dizziness, fainting, increased pain or bruising. Acupuncturists caring for women during pregnancy and birthing have an additional responsibility to provide treatment that is safe to the pregnant woman and her foetus or baby.

There is debate within the acupuncture literature to the existence of forbidden acupuncture points (BL60, BL67, CV4 and SP6) and whether these acupuncture points should be avoided during pregnancy (Betts and Budd, 2011; da Silva et al., 2011). Concerns have been raised that stimulation of these points may lead to an increased risk of miscarriage or early labour. No evidence has been found so far of mechanisms for these adverse events (Cummings, 2011), which are based on traditional understanding. This chapter describes the evidence for acupuncture to stimulate labour for women with postdate pregnancies. It is important to highlight that uterine contractions are normal during pregnancy, particularly during the later weeks of the third gestation of pregnancy.

Data on the safe use of acupuncture during pregnancy has been informed by clinical research, with studies reporting side effects or adverse events relating to treatment, for example pain, discomfort, feeling faint, tired or relaxed etc. However, in relation to pregnancy it is also important to collect both maternal and neonatal outcomes. Data on safety can be sourced from clinical trials which can be a good source of data because they should provide routine monitoring of adverse events within the trial.

Data on the safety of acupuncture in pregnancy has been reported in trials evaluating acupuncture to treat nausea, back pain, induction of labour, pain relief in labour and moxibustion for the management of breech presentation. Trials in the first trimester of pregnancy have been mostly limited to the treatment of nausea and vomiting in early pregnancy. One large randomised controlled trial (RCT) found no difference in the incidence of adverse perinatal outcomes, congenital abnormalities, pregnancy complications or neonatal outcomes for those women receiving acupuncture compared with standard care (Smith et al., 2002b). Data from a systematic review of acupuncture to treat back pain found no serious adverse events associated with acupuncture (Pennick and Young, 2007). A review of adverse events during pregnancy are described as mild and transient, with serious events occurring rarely (Park et al., 2014). In these individual trials minor adverse events, such as local pain or bruising, sweating, nausea, weakness and tiredness, were reported. In one of these trials acupuncture administered with strong stimulation led to minor adverse complaints (pain, initially worsening of pain) from subjects, but these had no observable adverse influences on the pregnancy, delivery or the foetus or neonate (Elden et al., 2008b). Cardiotocography (CTG) recordings made during the antenatal period were all normal.

### Clinical points

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The available studies find no evidence that correctly performed acupuncture or moxibustion pose any risk to pregnancy or the unborn foetus.

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Although little data have been reported on the safety of moxibustion, there is no evidence from trials reporting on maternal and neonatal outcomes that moxibustion is associated with a higher risk of adverse outcomes compared with standard care alone. There is no evidence of differences comparing moxibustion with any other technique, with respect to rates of caesarean section, premature births, Apgar score less than 7 at 5 min, operative deliveries (by vacuum or forceps), or premature rupture of the membranes. The safety of moxibustion has been assessed by antenatal CTG in a sub group of women from one trial (Guittier et al., 2011) with no short term alterations

detected following the application of moxibustion to BL67. Acupuncture given to women during childbirth and for the management of labour has also not been associated with any evidence of increased adverse effects to the mother or baby (Smith et al., 2008, 2011; Smith and Crowther, 2004; Modlock et al., 2010; Asher et al., 2009; Harper et al., 2006).

## Nausea and vomiting of pregnancy

The treatment of nausea in early pregnancy using acupuncture or acupressure may be useful for some women; see also Chapter 22. The most recent systematic review included 14 trials and 1655 women (Helmreich et al., 2006). Studies recruited women during the first trimester of pregnancy, mostly between 8 and 11 weeks of pregnancy when symptoms increase in severity and frequency and before symptoms start to resolve spontaneously. The review included acupressure (using finger pressure or a wristband with a button), manual acupuncture and electrical stimulation. This review reported a reduction in nausea (relative risk (RR) 0.55, 95% CI: 0.38–0.77) and vomiting (RR 0.45, 95% CI: 0.32–0.63) for all forms of acupressure stimulation compared with a control group.

The regime administered in the acupressure trials using finger pressure varied from 5 to 30 min, four times daily or as needed, from 4 to 7 days. In trials using bilateral wristbands, the treatment period varied from 3 to 14 days. In this review four trials administered acupuncture. The frequency and regime of acupuncture treatments varied from 30 min for three times daily for 2 days, to once weekly for 20 min for 4 weeks. Acupuncture trials have reported stimulating point PC6, and two other trials used several other points (including ST34, ST36, ST44, SP4 and CV12) and other points based on a traditional Chinese medicine (TCM) diagnosis.

The review found no evidence that acupuncture reduced vomiting in three trials (RR 1.01, 95% CI: 0.88–1.17). The effect on nausea was less clear due to different study designs used in the trials. One trial found no difference in nausea at the end of the intervention, with nausea reported by 25% (7/28) in the acupuncture group and 33.3% (9/27) in the control group (Knight et al., 2001). A second trial included four study groups (treatment based on TCM diagnosis, PC6 only, penetrating sham acupuncture and usual care only) and examined whether acupuncture (both traditional acupuncture and PC6 acupuncture only) was better than sham acupuncture or no acupuncture in reducing the frequency, duration, amount and distress from nausea, dry retching and vomiting, and improved the health status of women in early pregnancy (Smith et al., 2002a). Women receiving a TCM diagnosis and given an individualised treatment reported less frequent and shorter periods of nausea, which caused less distress, compared with women in the usual care group at the end of the first week of treatment (mean score 5.0 vs. 6.1,  $p < 0.05$ ). Women in the TCM group (13, 9%) were more likely to be free from nausea compared with women in the usual care group (4, 3%) (RR 0.93, 95% CI 0.88–0.99). On completing the second week of the trial, women who received TCM reported lower nausea scores compared with women in the usual care group (mean 4.6 vs. 6.0,  $p < 0.001$ ), as did those who received PC6 acupuncture (4.8 vs. 6.0,  $p < 0.05$ ). This improvement in nausea continued for women receiving TCM ( $p < 0.001$ ) and PC6 only ( $p < 0.01$ ) into the third week compared with women in the usual care group. From the third week, women in the sham acupuncture group ( $p < 0.01$ ) also reported lower nausea scores compared with women in the usual care group (this may have indicated a time-related placebo effect occurred for some women in the sham group). In the final week of the study, improvements in nausea continued for women in the three groups compared with usual care only. In this trial (Smith et al., 2002a) the inclusion of a TCM group provided an opportunity to practice acupuncture as in a clinical setting, rather than reliance solely on the specific point PC6. Whether there is an additional benefit from treatment administered after a full TCM diagnosis remains less clear from the research to date. Further studies are needed.

## Clinical points

Moderate evidence suggests that acupuncture is effective for nausea and vomiting of pregnancy, but it is not established whether this is a specific needle effect.

Patients given acupuncture to treat mild to moderate nausea and infrequent vomiting can respond well if they are able to present twice weekly for a minimum of 2 weeks. Treatment of hyperemesis requires more frequent acupuncture, and can be less responsive. A crossover study undertaken in Sweden treated 35 women with hyperemesis using deep needle penetration of PC6 or superficial placebo acupuncture (Carlsson et al., 2000). Treatment was administered over eight consecutive days for each participant, treatment was administered on days 1 and 2, three times daily, followed by a 2 day wash out period over days 3 and 4, followed by two additional days of treatment on days 5 and 6. The study demonstrated a faster reduction of vomiting and reduced vomiting episodes following active acupuncture. A strategy to commence acupuncture early after symptoms become troublesome may lead to better outcomes. Frequently women will be struggling with food choices, and presenting women with written information on bland food options with advice to try to eat small frequent snacks is useful. Symptoms of tiredness and nausea frequently go hand in hand and can exacerbate each other. It is important to provide encouragement to rest as this can be instrumental in influencing the effectiveness of treatment. The therapeutic alliance and interpersonal skills of an acupuncturist are important when working with women who have struggled for weeks feeling awful. For women with severe symptoms home visits should be considered. Some women are keen to avoid being admitted to hospital and sometimes may not realise they are dehydrated. Whilst attending women it is important to monitor for signs of dehydration, and if apparent, recommend immediate referral to their maternity emergency department or maternity provider for attention.

## Mood disorders during pregnancy

For the majority of women pregnancy is a time of emotional wellbeing. However, a meta-analysis of 21 studies suggests that the mean prevalence rate of depression across the antenatal period is 10%, ranging from 7.4% in the first trimester to a high of 12.8% in the second trimester (Bennett et al., 2004). It is important to be alert to the symptoms of depression that may arise during the antenatal period and to refer the women for professional help if symptoms persist beyond 2 weeks. Depression during the antenatal period increases the woman's risk of postnatal depression. Options for treating depression during pregnancy are limited, and many women are concerned about the potential side effects of medication, and express a reluctance to use medication particularly during early pregnancy. Therefore non-pharmacological approaches to manage symptoms of depression have great potential value.

There is a growing body of evidence for the effect of acupuncture in depression (Smith et al., 2010). However, there are few RCTs evaluating the role of acupuncture to assist with the management of depression during the antenatal period. A pilot RCT of 61 women with major depression in the antenatal period compared acupuncture with massage and a non-specific acupuncture control (this involved the application of points not specific to the treatment of depression) (Manber et al., 2004). At the end of the acute phase of treatment there was a statistically significant response to treatment from the acupuncture group 68% versus non-specific group 48% and massage 31%. These study findings were encouraging and found treatment responses from women receiving acupuncture similar to those of conventional treatments for depression (Manber et al., 2004). A more recent RCT ( $n=150$ ) compared an 8 week intervention of acupuncture, with two active controls (Manber et al., 2010). This included a non-specific acupuncture group administering non-specific acupuncture points for the treatment of depression and a massage group. Treatment was administered twice a week for 4 weeks, and weekly for an additional four treatments, and

lasted 25 min. Acupuncture was tailored to the individual based on a TCM diagnosis, and the control group received acupuncture at points not used in depression. Seven to twelve acupuncture points were needled at each session in both groups. The third group received massage consisting of Swedish massage provided in a standardised fashion and included effleurage and petrissage strokes. Results indicated that women who received acupuncture specific for depression demonstrated a greater reduction in depression severity scores compared with the acupuncture control ( $d=0.46$ , 95% CI 0.01–0.92), but there was no difference to the massage control. Acupuncture was associated with a clinically significant remission rate of 29%. Further detailed information on diagnostic approaches to the treatment of depression in pregnancy used in these studies is described elsewhere (Schwyner et al., 2001).

Although these studies were small, the results are encouraging and suggest acupuncture could be a useful treatment option for pregnant women. Additional studies during pregnancy are needed to build the evidence base.

## Back and pelvic pain

Low back pain and pelvic pain is a common complaint during pregnancy, experienced by up to 68% of women. It frequently arises in response to the physiological changes associated with pregnancy, such as altered posture with the increased lumbar lordosis and loose ligaments, and may be exacerbated by risk factors including previous back pain and physical strain. Pain usually increases as the pregnancy advances and consequently can interfere with activities of daily living such as sitting, walking, going to work and may disturb sleep. Frequent advice given to manage this pain includes exercises, frequent rest, hot and cold compresses, a supportive belt, massage, chiropractic, aromatherapy, relaxation, herbs, yoga, Reiki, pharmacological pain relief as well as acupuncture.

Three trials have been included in two systematic reviews of acupuncture to treat pelvic and back pain (Ee et al., 2008; Pennick and Young, 2007). The most recent review included two small trials and one large trial of acupuncture (Ee et al., 2008). The treatment protocols used in these studies were heterogeneous. Treatment frequencies varied between 1 and 2 times per week. Acupuncture point selection included auricular points, classical acupuncture points on the sacrum, bladder points (BL22–26), as well as peripheral points (BL60, SI3 LR3 and GV20), and extrasegmental points to neurological innervations. Only one trial in the review was of high methodology quality (Elden et al., 2005). This trial found after 1 week of treatment, those who received acupuncture had less pain in the evening than the stabilising exercise group, with the percentage reduction of pain 46% in the acupuncture group, 20% in the exercise group and 6% in the control group. In the other two trials, women receiving acupuncture reported less intense pain compared to women in the control groups.

Since publication of the systematic review an additional trial of acupuncture compared with non-penetrating sham acupuncture ( $n=115$ ) has been reported (Elden et al., 2008a). This trial found no significant difference in pain outcomes between groups. At the end of the trial there were more women in the acupuncture group compared with the sham control who were kept in regular work ( $n=28/56$  vs.  $16/57$ ,  $p=0.041$ ). Women in the acupuncture group were better able to engage in daily living activities compared with the sham control ( $n=44$  vs.  $55$ ,  $p=0.001$ ); however, there was no significant difference in function between groups. There were also improvements in quality of life for both groups. The dose of acupuncture in this trial differed from earlier studies with an increased number of treatments and acupuncture points administered.

## Clinical points

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Moderate evidence suggests acupuncture is effective for the management of back and pelvic pain in pregnancy.

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## Moxibustion for breech presentation

Three to four percent of babies at term are in a breech presentation (Hutton et al., 2002) and many are delivered by caesarean section. From 37 weeks external cephalic version (ECV) is used to try and turn a breech foetus to the cephalic (head down) position by externally rotating the foetus around the mother's abdomen. However, ECV is unsuccessful in approximately 40% of attempts, has low acceptability attributed to fear of pain, and concerns about the safety of the technique. Moxibustion is a technique which generates heat by burning a herbal preparation containing *Artemisia vulgaris* (mugwort). To promote cephalic version, moxibustion is applied over the acupuncture point Bladder 67 (BL67) (located on the fifth toe).

There is a growing body of evidence from clinical trials evaluating the effectiveness of moxibustion. The most recent meta-analysis (Vas et al., 2009) included data from six studies, with 1087 subjects, and compared moxibustion with observation or postural methods. The review reported a rate of cephalic version among the moxibustion group of 72.5% versus 53.2% in the control group (RR 1.36; 95% CI 1.17–1.58). There is significant clinical heterogeneity between study treatment protocols of these trials. Interventions vary in the frequency and duration of applying moxibustion, and the mode of stimulation, although all studies used point BL67. Studies indicate moxibustion is mainly applied prior to 37 weeks gestation, for 10–14 days. There is an increasing tendency to use smokeless moxa sticks to assist with patient compliance, and most women self administer moxa at home following initial instruction. Moxa is generally held 2–5 cms above BL67 until the warmth becomes uncomfortable; the stick is then moved away and then moved back into position until the heat becomes uncomfortable. Moxa is usually applied once or twice a day for either 20–30 min in total (10–15 min each side). In most cases moxibustion of BL67 is used alone, although in some cases additional acupuncture points may be selected. A possible mechanism explaining how moxibustion may promote cephalic version is discussed later. The addition of acupuncture to moxa was examined in a recent trial (Coulon et al., 2014). This study of moxibustion plus acupuncture administered to BL67 or an inactive laser over six sessions found no difference between groups.

### Clinical points

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Moderate evidence shows that moxibustion to BL67 is effective in converting breech to vertex presentation. The physiological basis is unknown.

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A qualitative study undertaken in Switzerland reported 10 out of the 12 women interviewed had used moxibustion, acupuncture or ECV to turn their babies (Guittier et al., 2011). Women using moxibustion perceive it to have a positive effect resulting in increased foetal movements, and increased positive maternal feelings described as relaxing, pleasant, safe and enjoyable (Mitchell and Allen, 2008). Further, women spoke of how the process involved with the application of moxibustion gave them the opportunity to focus on their pregnancy, how it helped them to connect with their baby, and provided an opportunity to spend time with their partner.

## Cervical ripening, induction of labour and augmentation of labour

Sometimes it is necessary to bring on labour artificially because of safety concerns for the mother or baby. However, there are concerns about the increasing use of medical interventions in childbirth, and international policy makers recommend strategies to promote normal birth and reduce

caesarean section rates. The role of acupuncture to ripen the cervix or to stimulate labour was initially reported in several case series and other observational studies. Two non-randomised trials have examined whether acupuncture could initiate contractions in women at term (Kubista et al., 1975; Theobald, 1973). An increase in the intensity of labour contraction frequency was observed in 31 women in the treatment group. In the control group no increase in labour activity was observed (Kubista et al., 1975). In the trial by Theobald (Theobald, 1973) four electrodes were applied to the skin of the abdomen to induce labour in the treatment group. Treatment was given to 27 women and compared with 102 women who were controls. In the treatment group 20 (77%) women gave birth on or up to 4 days before the estimated date of confinement, compared with 47 (46%) in the control group.

Over the last decade there have been several clinical trials, and a review of the effectiveness of acupuncture focuses on clinical trial data. The role of acupuncture to induce labour has been summarised in a systematic review (Smith et al., 2013). This review included 14 trials (2220 women) and found some evidence of a change in cervical maturation for women receiving acupuncture compared with the sham control (MD 0.40, 95% CI 0.11–0.69, one trial, 125 women), and when compared with usual care (MD 1.30, 95% CI 0.11–2.49, one trial, 67 women). A description of study characteristics is presented in Table 33.1.

The length of labour was shorter in the usual care group compared with acupuncture (MD 0.67, 95% CI 0.18–1.17, one trial, 68 women). There were no other statistically significant differences between groups. Few studies reported on clinically relevant outcomes, and further research is required.

## Pain management in labour

The role of acupuncture to assist with the management of pain during labour has been evaluated in nine RCTs and assessed in two systematic reviews (Smith et al., 2011; Cho et al., 2010). Although both reviews agree there is a need for further research with improved designs, the most recent review (Smith et al., 2011) concluded that acupuncture and acupressure may have a role with reducing pain, increasing satisfaction with pain management and less use of pharmacological methods. There is no evidence of acupuncture reducing the intensity of pain compared to a sham control, however, acupuncture compared to no treatment found women reported less intense pain compared with women receiving no intervention (SMD –1.00, 95% CI –1.33 to –0.67) (Huang et al., 2008). Acupuncture increased satisfaction with pain relief in labour compared with the sham control (RR 2.38, 95% CI 1.78–3.19) (Hantoushzadeh et al., 2007), and women receiving sterile water injection were more satisfied with pain relief from water injection than with acupuncture (MD 18.60, 95% CI 11.54–25.66) with satisfaction rated along a 100 mm VAS scale (Martensson et al., 2008). Use of pharmacological analgesia was lower in the acupuncture group compared with standard care (RR 0.68, 95% CI 0.56–0.83) (Borup et al., 2009; Nesheim et al., 2003; Ramnero et al., 2002). A trial from Sweden compared 40 min of manual acupuncture, electro-acupuncture or standard care alone and found no difference in pain relief between groups (Vixner et al., 2014). However, fewer women allocated to electro-acupuncture required an epidural compared to manual acupuncture or usual care alone. Acupuncture protocols mostly used individualised treatments; the most frequently used points were SP6, LI4, BL23, BL32, HT7, GB34, LR3 and ST36. Many of these trials were undertaken in Europe, and the acupuncture was administered by midwives who had received acupuncture training. The duration of needling varied from 20 min to needles being taped in for the duration of labour. Most trials included only a few clinical outcomes and omitted safety outcomes. In clinical practice, supporting women with acupuncture to assist with pain management can be logistically difficult due to the unpredictability of time of onset of labour and availability of support. Midwives who have received appropriate training in acupuncture are well placed to provide support to women.

TABLE 33.1 ■ RCTs to promote cervical change and induction of labour

References	Groups (n), (country)	Treatment regimen	Control group
Asher et al. (2009)	89, acupuncture (n=30), sham (n=29), control (n=30) (USA)	LI4, SP6, BL32, BL54. MA, 30 min. Maximum 5 treatments over a 2-week period	Shallow needling at non-acupuncture points on hands, legs and lower back, 30 min. Second control group received prenatal care only
Gaudernack et al. (2006)	Acupuncture (48), standard care (52) (Norway)	LIV3, ST36, CV4; plus other points, total (9) TCM diagnosis, 20 min	Conventional medical treatment i.e. prostaglandins and or oxytocin
Gaudet et al. (2008)	16, acupuncture or sham control (Canada)	EA at SP6, ST43, BL60, at 1–2 Hz for 30–45 min, and MA at LI4. Two sessions	Adjacent sites, non-points, EA
Gribel and Coca-Velarde (2011)	72, acupuncture or misoprostol	Surface electro-stimulation to LI4, ST36, LIV3, SP6, BL23, BL32. Electro-stimulation (5 or 50 Hz), 30 min. Every 7 h up to 3 sessions in a 24 h period	Misoprostol (25 mg intravaginally; every 6 h; up to 4 tablets) within 24 h
Harper et al. (2006)	56, acupuncture or standard care (USA)	Bilateral EA to LI4, SP6, BL31, BL32, 2 Hz, 30 min. 3 out of 4 consecutive days	Routine care (not specified)
Long (1994)	400, acupuncture or rivanol (China)	Auricular acupuncture: Inter Genitals, Sympathetic, Shenmen, Liver, Yuanzhong and Adrenal gland, using a mustard seed or a pill with adhesive plaster. Points pressed by the woman until the points felt warm	The control group received 1% rivanol
Mackenzie et al. (2011)	105, MA, EA, sham MA, sham EA or no treatment in the (UK)	MA and EA LI4, SP6, BL60, BL67, 30 min. EA at 2-Hz, sufficient to cause non-painful muscle contractions	Sham acupuncture inserted at shallow sites adjacent to specific acupuncture points and insufficient to provoke an unusual sensation. Sham EA connected to inactivated electrical stimulator

Martinez et al. (2004)	50, acupuncture or no intervention (Philippines)	SP6 stimulated bilaterally for 2 min	The control group received no intervention
Modlock et al. (2010)	125, with a postdate pregnancy, acupuncture or sham (Denmark)	MA at BL67, LI4, SP6, GV20, 30 min, needles were stimulated every 10 min. Two treatments	Non-invasive Park sham needle at real acupuncture points BL67, LI4, SP6, GV20
Rabl et al. (2001)	56, at term acupuncture or no acupuncture (Austria)	MA at LI4, SP6 at 2-day intervals, 20 min	Routine care. If the woman was undelivered 10 days after her EDC labour was induced
Romer et al. (2000)	553, acupuncture or sham (Germany)	MA at ST36, SP6, GB34, BL67, 20 min weekly from 36 weeks until delivery	MA at non-specific points including GV20, PC6, HT7
Selmer-Olsen et al. (2008)	106, acupuncture or standard care (Norway)	MA at CV4. Other points based on TCM diagnosis. Spleen <i>qi</i> deficiency, BL20, SP6, ST36. Liver <i>qi</i> stagnation, BL18, LIV3, LI4. Kidney <i>qi</i> deficiency, BL23, KI3. Additional points when appropriate, GV4, GV20, HT7, BL15, LU7, BL32, PC6, TH6. All 30 min. Additional treatment next day if not in labour	Standard care
Smith et al. (2008)	364, with a planned induction for postdates, acupuncture or sham (Australia)	MA at LI4, SP6, BL31, BL32, ST36, LIV3. Plus points from TCM diagnosis, e.g. KI7, BL20, BL21, LR3, 30–40 min with strong stimulation and <i>de qi</i> . Two treatments	Minimal insertion and stimulation at non-points on sacral area, hand, foot, a point below the knee and lower leg
Tremeau et al. (1992)	128, late pregnancy (effect on cervical maturation) (France)	MA at CV2, CV3, CV4, LR3, BL60, GB34, ST36, LI4, SP6, BL67, 20 min. Three treatments	Needle pricks at sites away from true points. A third group received usual care

MA, manual acupuncture (with stimulation to elicit *de qi*, unless otherwise stated); EA, electro-acupuncture.

## Clinical points

Moderate evidence suggests that acupuncture used for labour pain reduces the requirement for other analgesics.

## Retained placenta

A retained placenta is described as a placenta requiring removal. This complication of the third stage of labour is the principal cause of postpartum haemorrhage. Active management may involve the administration of a prophylactic oxytocic drugs after delivery of the baby, early clamping and cutting of the cord and controlled cord traction of the umbilical cord.

There is little research examining the use of acupuncture for this clinical complication. A non-randomised controlled study of women at term with placental retention compared the release of the placenta in 45 women receiving manual removal and 30 women receiving acupuncture to stimulate the release of the placenta (Chauhan et al., 1998). In the acupuncture group 83% of women delivered the placenta within 20 min following acupuncture. In the control group, 23 (51%) women had a third stage lasting 1–1.5 h, and 22 women a third stage lasting longer than 90 min. Six women receiving acupuncture had complications compared with 26 women in the control group. Administering acupuncture at this time is challenging, although trained midwives are well placed to address this complication. Further research is required.

## Postpartum disorders

Breast engorgement can occur if the baby removes less milk from the breast when feeding than the amount that the mother produces. As well as causing breast engorgement, this can result in problems such as plugged milk ducts, breast infection and insufficient milk supply. The distress associated with breast engorgement may mean that women initiating breastfeeding may not persevere beyond the first few days after the birth. The evidence base for many pharmacological and non-pharmacological techniques is not well established.

Three clinical trials of acupuncture address breastfeeding support. Two studies from Sweden included 293 women, and both have been described as having a moderate risk of bias. Kvist et al. (2004) applied acupuncture points HT3, GB21 in one treatment group, and a second treatment group received HT3, GB21 and SP6 (Kvist et al., 2004). Acupuncture was applied by acupuncture midwives who had attended a 4-day training course. Needles were inserted to a depth of 3–5 mm and *de qi* was obtained. Few clinical outcomes were reported to determine the effect of acupuncture; however women in all groups were satisfied with the care they received. In their subsequent study Kvist et al. (2007) applied the same treatment protocol. The study found women receiving acupuncture were less likely to have an abscess and not be prescribed antibiotics compared to women receiving usual care, although these differences did not reach statistical significance. The trial also found that women receiving acupuncture at days 3–5 following treatment reported fewer symptoms.

Neri and colleagues (Neri et al., 2011) reported preliminary data from a randomised trial of 90 women who had been referred to a breastfeeding clinic due to insufficient milk supply. A semi-structured formula approach to acupuncture treatment was used. This included specific points relating to the breast ST18 and CV17 and milk ejection SI1. If women presented with symptoms such as fatigue, a pale complexion and a low appetite (Qi and Blood deficiency), additional points ST36, SP6, BL20 were added. For irritability (Liver Qi stagnation) LR3 and PC6 were added. Needles were inserted to a depth of 10–30 mm, with *de qi*; needles were left in place for 30 min. Acupuncture was applied twice weekly for 3 weeks. The results demonstrated higher rates of exclusive breastfeeding in the acupuncture group compared with no acupuncture control group at 3 weeks (98% vs. 60%,  $p=0.03$ ), and at 3 months (35% vs. 15%,  $p=0.03$ ).

## The mechanism of acupuncture in pregnancy

Few studies have examined the potential mechanisms of acupuncture for the complaints in pregnancy treated by acupuncture. The majority of acupuncture points are either connected to, or located near, neural structures; this suggests that acupuncture stimulates the nervous system.

A mechanism underlying acupuncture to induce labour is speculative at this stage but may involve stimulation of the uterus by hormonal changes or by the nervous system. Parasympathetic stimulation close to term has also been shown to have an influence on the uterus (Bell, 1972). Stimulation of acupuncture points is known to increase the discharge of thalamic nuclei and the hypothalamic anterior pituitary system (Liao et al., 1979). It is hypothesised that acupuncture neuronal stimulation may increase uterine contractility either by central oxytocin release or by parasympathetic stimulation of the uterus (Tempfeer et al., 1998), without influencing locally active factors such as IL8 (interleukin-8) and PGF2 (prostaglandin-F2) either by central oxytocin release or by parasympathetic stimulation of the uterus (Tempfeer et al., 1998).

Explanations of how acupuncture may assist with reducing back pain and labour pain have in general been attributed to a role of the autonomic nervous system, neuro-endocrine system and opioids. The mechanisms of acupuncture for pain control are discussed in [Chapter 3](#).

An explanation of how moxibustion may facilitate cephalic version is speculative at present. Moxibustion is applied close to the skin until it produces hyperaemia from local vasodilatation. The general mechanism is proposed to be a combination of thermal (infrared radiation) and aroma (fume) of the materials used stimulating physiological responses (Yamashita et al., 2001). Moxa sticks have been shown to emit primarily long-wavelength infrared radiation (IR-C) indicating that moxa mainly affects the skin where heat receptors are located (Kim et al., 2011; Pach et al., 2009). Due to the limited skin penetration of IR-C, thermal effects on internal organs are more likely to arise from reflex mechanisms (Kim et al., 2011). It has been proposed that moxibustion might stimulate adrenocortical activity leading to an increase in the production of placental oestrogens, potentially leading to greater sensitivity of the myometrium, and changes in the relationship between F and E prostaglandins. This changed relationship may be accompanied by a reduction in type E prostaglandins, where type F prostaglandins would remain unchanged resulting in an increase in uterine contractions and foetal activity leading to version of the foetus (Cooperative Research Group of Moxibustion Version of Jiangxi Province, 1984). Alternatively, the stimulation of heat may result in reduced muscle tone which may facilitate cephalic version.

## Concluding comments

There is substantial interest by women and their health care provider to the use of acupuncture and other complementary therapies to improve maternal health outcomes, and there is significant enthusiasm by acupuncturists to apply their treatment. The evidence base for acupuncture however remains relatively small, and although there are areas where research demonstrates improved outcomes, for many clinical conditions there remains insufficient evidence to demonstrate its effectiveness. However, there is no evidence of harm.

Among these clinical studies there is little discussion of how well the treatment regimens being evaluated reflect clinical practice. In reality there is variation in acupuncture practice reflecting the diversity of approaches including TCM, Western medical acupuncture, Five Element acupuncture, Japanese acupuncture, Korean acupuncture and an integration of paradigms. Clearly there is a need to strengthen and build the evidence base. The limitations of previous studies highlight methodological areas which must be addressed, but also new directions are needed to move this area forward to examine the role acupuncture in pregnancy.

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# Acupuncture in cancer and palliative care

C. Rubens ■ J. Filshie

## CHAPTER OUTLINE

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## Introduction

Acupuncture is being used increasingly alongside conventional medical treatment for pain and symptom management in the palliative care setting (Filshie and Thompson, 2009; Garcia et al., 2013; Towler et al., 2013). In a recent survey of hospices and specialist palliative care services in the United Kingdom, acupuncture was being used by 59% of those who responded (Leng, 2013). People with cancer and other life-limiting conditions often undergo aggressive medical and surgical treatments in an attempt to control their disease. However, some treatments can be almost as burdensome as the actual disease. Palliative care aims to help control patients' symptoms rather than curing their disease and considers wider issues than the disease process itself. It supports patients physically, psychologically, emotionally and spiritually, focusing on what is troubling them on a day-to-day basis as they live with potentially life-limiting conditions. As acupuncture has become more widely acceptable due to its increasing evidence base, its use in patients with cancer and the palliative care setting has gradually become more widespread.

As patients with cancer are living longer, they are increasingly turning to complementary therapies to help cope with the burden of the illness. Acupuncture can offer such patients a relaxing treatment with minimal side effects yet numerous beneficial effects. It may be used to treat symptoms where medical treatments have either not worked or were not tolerated, or to counteract the effects of these treatments. This chapter will discuss the symptoms for which acupuncture is most helpful in cancer care, possible mechanisms of action and available evidence as well as areas of ongoing research. Most of the clinical and research work in this area focuses on cancer, but other life-limiting conditions are also discussed which may also be amenable to treatment with acupuncture.

## Clinical aspects

Before treating a patient with cancer for the first time it is important to take a full medical history including a detailed pain history if appropriate and a full social history. It is useful to know if they have previously had acupuncture and what their response was. A clinical examination appropriate to the presenting complaint should be performed including an assessment of the psychosocial state of the patient. It is helpful to discuss the likelihood of success of the treatment at the outset. Acupuncture can then be used to treat the presenting symptom if appropriate and any other symptoms that have become apparent during history taking that are amenable to acupuncture. In an audit of 150 patients attending an out-patient clinic in a cancer hospital, up to six symptoms were treated in any one patient, and only 20% of patients were treated for one symptom alone (J. Filshie and C. Rubens, paper in preparation, 2015). Acupuncture should be used as a therapy alongside appropriate medication and psychological support and ongoing communication between different clinicians involved is vital.

Initially an empirical treatment can be given with subsequent treatments intensified or reduced according to responses to previous treatments. Needles of smaller diameter than those used on the general population are used in this group, and they may be inserted more superficially. A typical treatment schedule would include 6 weekly treatments each lasting for 10–20 min. The length of pain relief tends to increase with each successive treatment which often results in patients reducing the amount of daily analgesic consumption. As the benefit is usually maximal after a complete course of treatment and tends to wear off over time, in some conditions, ‘top-up’ treatments can then be given to maintain the effects of treatment. Top-up treatments can be given at increasing intervals tailored according to the level of symptom control. A variety of methods have been introduced to help prolong effects of acupuncture after an initial course, including massaging semi-permanent indwelling needles in patients with dyspnoea and teaching self-needling in patients with hot flushes. These methods can also be used to augment treatment where only short-lived symptom relief is obtained.

It has been noticed that patients with pain and advanced disease need multiple and continuing ‘top-up’ treatments to maintain adequate analgesia, with some patients experiencing a reduced response to acupuncture over time (Filshie and Thompson, 2009). An inverse relationship has been noted between tumour burden and length of response to acupuncture for pain control with those with the greatest tumour burden or more active disease getting the shortest benefits (Filshie and Redman, 1985). Any tolerance in a patient who has previously responded well to acupuncture is considered an indication for further investigation for possible recurrence. In one audit of patients exhibiting tolerance, 17 out of 27 patients had developed further metastases (Filshie, 1990). A potential mechanism for tolerance is that endogenous opioid production may be maximal in cancer patients preventing any greater response when treated with acupuncture (Filshie and Thompson, 2009). Observations in animal models have also shown that the opioid antagonist angiotensin II and cholecystokinin (CCK) are released by prolonged electroacupuncture (EA) (Wang and Han, 1990; Zhou et al., 1993). Interestingly, tolerance to acupuncture for advanced cancer-related dyspnoea, hot flushes, xerostomia and fatigue is much less likely to occur, in contrast to pain symptoms (J. Filshie, clinical observation).

## Clinical points

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Tolerance to acupuncture for pain relief can occur in advancing disease, and any reduction in response to previously effective acupuncture treatments should trigger prompt referral for further investigation.

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## Cancer pain and cancer-related pain

A large proportion of patients with cancer suffer from significant pain despite appropriate titration of analgesics and co-analgesics (Filshie, 1990). The side effects from these medications can become overwhelming, and many patients like to try non-drug treatments such as acupuncture to help control their symptoms. In practice acupuncture is often used as an adjunct to analgesics and may enable some patients to reduce or abolish their dose and side effects. Acupuncture can also improve mobility, and this effect may precede pain relief and can enable proper positioning for radiotherapy and activities involving reaching such as driving.

Pain may be a direct result of the cancer itself, a consequence of treatment for cancer or entirely unrelated to the cancer. It is important to try to identify the cause of pain which may be due to a combination of causes and may be nociceptive and/or neuropathic in origin (Filshie and Thompson, 2009). Causes of pain related to tumour growth include bone pain, nerve pain, soft tissue infiltration or visceral involvement. Pain related to treatment may be due to surgery, radiotherapy or chemotherapy or a combination of these. Surgery such as mastectomy, thoracotomy or radical neck dissection are well known to cause chronic pain states with pain months or years later and is a significant cause of morbidity in this group (Macrae, 2001). Indeed thoracotomy and mastectomy are among the most frequent conditions to cause chronic pain after surgery with only amputation having a greater incidence (Kehlet et al., 2006). A significant number of patients also have myofascial pain.

Acupuncture is used to treat pain in cancer patients caused by the disease itself or more usually a consequence of one or more of the following treatments such as surgery, radiotherapy and chemotherapy.

## CLINICAL APPROACH

When considering point selection several approaches may be used, and it is helpful to first consider whether the patient would be better treated sitting or lying down. Examination for trigger points may reveal pain of myofascial origin which can be successfully treated and is common in cancer patients. Segmental points are used, where a needle is inserted into an area innervated by the same spinal segment as the disordered structure under treatment. A paravertebral approach appropriate to the disordered region is usually chosen, often aiming to add concurrent sympathetic blockade, e.g. T1–T2 (head and neck), T1–T5 (chest and arm) and L1–L2 (lower back and limbs). Tender points and selected common traditional points such as LR3 and LI4 can also be added to the mix if there is no contraindication to use (Fig. 34.1).

It is hard to accurately quantify the ‘dose’ of acupuncture as it is influenced by numerous factors including length of treatment, the number of needles, depth of needle insertion, needle thickness and the degree and mode of stimulation. However, it has been noted that cancer patients are often ‘strong reactors’ requiring shorter gentler treatments (Mann, 2000). This must be taken into account when considering the initial and subsequent ‘dose’ of acupuncture being given during a treatment especially as there are wide variations in techniques used by different acupuncture practitioners.

Acupuncture sessions can offer patients with cancer a chance for personal reflection about their condition in a calm environment. It is a more gentle and natural treatment than cancer therapy and can help to empower patients both emotionally and physically. In an audit of breast cancer patients a reduction in pain, pain behaviour, distress, depression and interference with lifestyle was seen (Filshie et al., 1997). In clinical practice acupuncture treatment is rarely given alone; it is usually combined with a therapeutic interview, both of which may help the patient. The specific effects of acupuncture combined with the opportunity for discussion with a supportive practitioner and the relaxing effects of acupuncture will all affect outcome of treatment (Filshie and Thompson, 2009).



**Figure 34.1** Treatment showing segmental and trigger points.

When selecting acupuncture points for pain, a combination of segmental and trigger points is used together with commonly used points for analgesia such as LI4. For pain and vascular problems in the head, neck, arm and breast, paravertebral points at C7, T1 and T2 are used, which appear to be interchangeable with sympathetic blockade and hence are often colloquially referred to as *sympathetic blocking points*. Trigger points and strong traditional points are also used plus other local points. For pain in the abdomen, low back and lower leg, paravertebral points L1–L5 are used, and sacral points are added for perineal pain. If an improvement in the circulation in the leg is required, paravertebral needling at L1 and L2 appear to give a *sympathetic block* too.

## Treatment-related pain

### RADIOTHERAPY

Problems after radiotherapy include radiation fibrosis of a nerve plexus and radiation myelopathy. Brachial plexus neuropathy may result from radiotherapy to the axilla, though regimens which include overlapping fields of radiation are inadvisable and uncommon these days (Hanley and Staley, 2006; Maher Committee, 1995). Pain may also be caused by infiltration by the tumour and rarely by a sarcoma which is secondary to radiation treatment given in the past.

### CHEMOTHERAPY

Chemotherapy-induced peripheral neuropathy (CIPN) affects 10–20% of patients. Conventional treatments includes anti-neuropathic pain medication. In addition, acupuncture has been found to reduce these debilitating symptoms (Donald et al., 2011; Wong and Sagar, 2006; Schroeder et al., 2012; Bao et al., 2011), possibly through release of endogenous transmitters including nerve growth factor (NGF), gamma-aminobutyric acid (GABA) and adenosine. Oncologists have altered dose scheduling more recently which has led to a reduction in the incidence of CIPN, but some agents such as bortezomib (Velcade) continue to give some of the worst symptoms in patients with multiple myeloma (Filshie and Rubens, 2011). In addition to the published approaches earlier, useful points include ‘*sympathetic blocking points*’ (T1–T5, L1–L2) plus distal points and commonly used traditional points, e.g. LI4, TE5, SP6 and LR3 (JF, personal observation).

## SURGERY

Several randomised control trials (RCTs) have shown a role for acupuncture in the management of pain in patients after various cancer-related operations (Mehling et al., 2007), including post-thoracotomy pain (Wong et al., 2006) and postgastrointestinal surgery (Kotani et al., 2001). Pain following neck dissection was significantly reduced by acupuncture in a recent RCT ( $n=58$ ) as was dysfunction and xerostomia (Pfister et al., 2010).

It is known that pain after breast surgery is common and that it persists over time (Macrae, 2001; Meretoja et al., 2014). Recent large studies of breast surgery cohorts have found the prevalence of breast pain to be between 29% and 47%, with up to 13% of those patients reporting their pain as severe. The pain is frequently neuropathic in nature and generally affects the ipsilateral breast, axilla and arm (Brummett, 2011). Other types of pain syndrome are described including phantom breast pain, pain in or around the scar and pain in the chest wall. Scar pain is common after mastectomy, and for hyperpathia in the breast and chest wall a wide surrounding acupuncture technique is used, often termed ‘surround the dragon’ (Fig. 34.2).



**Figure 34.2** Surround the dragon circling technique of needling.

Breast surgery related pain may be caused by biopsy, wide local excision, axillary sampling or axillary dissection, mastectomy or mastectomy and reconstruction, e.g. implant only, latissimus dorsi flap or deep inferior epigastric perforator flap. Intercostobrachial nerve damage is common following axillary dissection, and a third of patients have chronic pain following breast surgery and half following reconstructive surgery (Wallace et al., 1996). Younger patients are more susceptible, and their quality of life may be adversely affected, in particular close contact with children and partners (Williams et al., 2010).

In one study patients were given acupuncture in the 2 weeks postbreast surgery with axillary dissection (He et al., 1999). The results showed a significant improvement in pain and increased arm abduction compared to a control group who had no acupuncture.

## AROMATASE INHIBITOR JOINT PAIN

There is emerging evidence to demonstrate the effectiveness of acupuncture for reducing joint pains commonly associated with aromatase inhibitors (AI) in women with breast cancer. Joint pains occurred in 47% of 200 patients (Crew et al., 2007). One RCT ( $n=43$ ) in women with early stage breast cancer compared true acupuncture with sham acupuncture for treating these symptoms (Crew et al., 2010). Pain scores and pain severity were lower in the true acupuncture group. The

two groups showed similar reductions in WOMAC and M-SACRAH scores, but this was probably due to the choice of control as the sham used superficial needle insertion at body locations not recognised as acupuncture points which would in itself have been an active treatment neurophysiologically. EA has also been shown to be effective in reducing joint pains in breast cancer patients experiencing joint pain as a result of adjuvant aromatase inhibitor treatment (Mao et al., 2009) and was found to be superior to a waiting list but equivalent to a sham control at 8 weeks, with benefit maintained in the EA group at 12 weeks (Mao et al., 2014). Acupuncture features in an algorithm devised by oncologists for treatment of aromatase inhibitor induced joint pains (Niravath, 2013).

## Clinical approach

Paravertebral C7–T2 (hands and arms); L1–L2 (feet); knee points including SP9, SP10, ST36, LR3, SP6; trigger points; and local points around the affected joints. It is important to remember to avoid needling a limb post lymph node dissection, e.g. axillary dissection/sampling.

Regular acupuncture treatments can permit a reduction in the analgesic intake as well as reducing the side effects of medication. Mobility may sometimes improve before a reduction in pain is seen. A course of acupuncture can enhance long term drug compliance in patients with AI-related joint pains.

## Evidence

Systematic reviews of acupuncture for cancer pain have not found sufficient evidence of effectiveness (Paley et al., 2011b; Lee et al., 2005), but these included only one high-quality RCT, which was positive (Alimi et al., 2003). This small trial ( $n=90$ ) used auriculoacupuncture and showed significant pain relief at 30 days and 2 months for neuropathic pain compared with the control interventions – needling or pressure beads at ‘incorrect’ auricular points. Two retrospective audits included 339 patients with pain symptoms not responding to conventional analgesia (Filshie and Redman, 1985; Filshie, 1990). Over 50% of patients obtained worthwhile analgesia after 3 weekly treatments and muscle spasm, bladder spasm and vascular problems were also helped significantly. Others have found similar results (Aung, 1994; Leng, 1999; Johnstone et al., 2002a).

EA given several times a day helped pain resistant to conventional means in patients with advanced cancer. This was very labour intensive, although over time treatments were needed less frequently (Wen, 1977). Paley et al. (2011a) suggest that a future potential use for acupuncture may be as an adjunctive treatment for breakthrough pain alongside ‘rescue’ doses of medication.

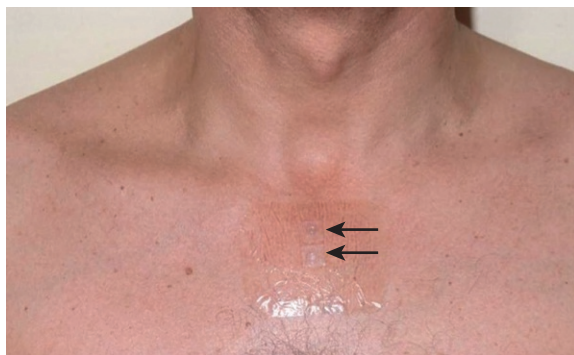
As acupuncture is widely used for pain in cancer patients, it is hoped that increasing numbers of relevant good quality RCTs will be undertaken to further inform clinical practice (Garcia et al., 2013).

## Non-pain symptoms

### BREATHLESSNESS

Breathlessness can be an extremely distressing symptom for patients towards the end of life. Conventional drug treatment including opioids, benzodiazepines and steroids may not adequately control symptoms and can cause unacceptable side effects such as drowsiness. Much of the published evidence on the use of acupuncture for breathlessness has been in patients who have chronic obstructive pulmonary disease (COPD). In an RCT of COPD patients, a significant improvement was seen in subjective breathlessness and 6-min walking distance in the acupuncture group compared with a control group although other objective measures were unchanged (Jobst et al., 1986). Other studies on acupuncture for COPD are described in Chapter 28. A prospective study of 20 patients with cancer-related breathlessness at rest showed marked symptomatic improvement in 70% and significant improvement in subjective scores of breathlessness, relaxation and anxiety at 90 minutes (Filshie et al., 1996). These effects were prolonged by using two indwelling studs at the top of the sternum which patients were instructed to massage before exercise or when their symptoms were particularly bad (Fig. 34.3). A reduction in respiratory rate was also noted in these patients during

treatment. Of note, these patients had previously failed to respond to steroids, opioids, nebulisers and oxygen therapy for their breathlessness. These points in the upper sternum are widely used by medical acupuncturists for cancer patients and are known as ASAD points as they are used for anxiety, sickness, analgesia and dyspnoea. They are used in numerous palliative care units in the United Kingdom and enable and empower patients to have an element of control over their symptoms. The studs are applied to cleansed skin and covered with a clear plastic dressing and may be left in place for up to 4 weeks at a time, changing the site slightly each time in the midline. They are then massaged on demand or prior to exercise or in the event of a patient having a panic attack.



**Figure 34.3** Two points in the upper sternum known as ASAD points are commonly used in the UK for treating anxiety, sickness and dyspnoea.

### Clinical approach

Paravertebral points T1–T5, trigger points in trapezius, LI4 and ASAD points are most commonly used.

A further pilot RCT looking at the effect of acupuncture on dyspnoea in 47 patients with lung and breast cancer found no difference compared with massaging of needle-less studs – which might not be inert (Vickers *et al.*, 2005).

An RCT comparing acupuncture with morphine and with acupuncture plus morphine was conducted on 173 patients with advanced cancer-related dyspnoea secondary to lung cancer or mesothelioma. They were all equally effective at alleviating dyspnoea, but the acupuncture significantly relieved anxiety, was more relaxing and was also morphine sparing. Acupuncture could therefore be recommended as a suitable alternative or adjunct for breathless patients with lung cancer or those experiencing opioid-related toxicity (O'Brien *et al.*, 2005).

The mechanisms of acupuncture for dyspnoea are unclear but may involve the sedative and central actions of endogenous opioid peptide release (Filshie and Thompson, 2009) and the anti-inflammatory actions of adrenocorticotrophic hormone release (Roth, 1997). The psychological effects of the reduction in anxiety may also contribute to a reduction in breathlessness (Mukaino *et al.*, 2005). Furthermore it is possible that the relaxation and relief of anxiety experienced during treatments using indwelling studs at sternal points may be due to release of oxytocin (Uvnas-Moberg *et al.*, 1993).

### NAUSEA AND VOMITING

Traditionally the point PC6 has been used for treating nausea and vomiting, and it is almost universally used for these symptoms in the West today. It is unusual for Western scientific acupuncture to be so specific in its point selection, but the practice derives from an observation by the late

Professor Dundee when he visited China and saw pregnant women receiving acupuncture at this point for morning sickness. He went on to conduct a number of studies using a single needle at this point which showed reductions in nausea and vomiting. Initially these studies demonstrated effectiveness for reducing perioperative nausea and vomiting (Dundee et al., 1989a), then using a modified approach they were used to demonstrate the synergistic effect of using acupuncture at PC6 to reduce chemotherapy-induced nausea and vomiting (Dundee et al., 1989b).

Nausea and vomiting are common symptoms at the end of life and are often multifactorial in origin, so establishing the underlying cause is important when considering drug and non-drug treatments. Causes of emesis include medication (e.g. opioids, antibiotics and iron), mechanical obstruction, gastric stasis and vagal nerve stimulation (e.g. from liver metastases or gastric irritation) (Twycross and Back, 1998). Pain can also cause nausea as can psychological symptoms such as fear and anxiety. Acupuncture may be used as an adjunct to anti-emetic medication or on its own. Acupuncture will not help in cases of genuine gastrointestinal obstruction, so this should be excluded before considering acupuncture as a treatment modality although it may improve symptom control in patients with partial obstruction (Filshie and Thompson, 2009). Indeed, some patients after brief training do very limited self-treatment at ST25, CV12 and CV6 which anecdotally limit the number of hospital admissions for partial obstruction. Often palliative care patients may wish to try acupuncture rather than take medication when they are feeling nauseous. Acupuncture has reduced nausea and vomiting postradiotherapy (Enblom et al., 2012).

Nausea and vomiting was the first area in acupuncture research to be formally systematically reviewed, showing acupuncture to be superior to a control group in 27 out of 33 RCTs (Vickers, 1996). There is now a substantial body of evidence available for the effectiveness of acupuncture for nausea and vomiting, particularly for postoperative nausea and vomiting and nausea in pregnancy. In a Cochrane review acupuncture at PC6 was shown to be as effective as anti-emetic drugs for preventing postoperative nausea and vomiting (Lee and Fan, 2009). This and other evidence is discussed in more detail in Chapter 21.

There is now a growing body of evidence for the effectiveness of acupuncture for chemotherapy-induced emesis. One high-quality RCT showed benefit for nausea and vomiting associated with high-dose chemotherapy for breast cancer compared with control groups (Shen et al., 2000). Ezzo et al. (2005) reviewed 11 trials for chemotherapy-induced emesis and found a significant reduction in acute vomiting with manual needling and EA. There was also a reduction in severity of nausea with acupressure, but no reduction in actual vomiting. It was concluded that acupressure is a low cost, convenient intervention for acute nausea that can be self-administered.

## Clinical approach

In palliative care, as well as PC6, a number of other points may be added due to the complexity of causes of nausea and vomiting. These include ST25, CV6, CV12 and ST36. Indwelling needles at ASAD points are also helpful for some patients giving them control of their symptoms and sometimes immediate relief from nausea by massaging these when they feel their symptoms coming on. Delayed nausea and vomiting after chemotherapy remains a challenge, and ways of prolonging these effects are yet to be shown.

Despite the wealth of evidence for the effectiveness of acupuncture in nausea and vomiting, little is known about the mechanisms of action. A number of possible mechanisms of acupuncture anti-emesis have been hypothesised including endogenous steroid release, oxytocin release, the contribution of CCK and the gastrointestinal site of 5-HT release with acupuncture. Acupuncture has also been shown to release endocannabinoids (Chen et al., 2009). Perhaps there is some contribution of endocannabinoid release affecting the anti-emetic response by acupuncture.

## HOT FLUSHES

Hot flushes are common in patients with breast cancer and also in men with prostate cancer. This is usually due to anti-oestrogen and anti-androgen drug treatment but may also be caused by women suddenly stopping hormone replacement therapy (HRT) following their cancer diagnosis. Treatment-related vasomotor symptoms can be very distressing and can contribute to patients giving up their anticancer treatment (Demissie et al., 2001). Two recent trials – ATTOM (Gray et al., 2013) and ATLAS (Davies et al., 2013) have shown that 10 years of tamoxifen significantly reduces the risk of recurrent cancer and mortality (Gray et al., 2013; Davies et al., 2013). And yet a number of studies have shown that more than 50% of women do not adhere to even 5 years of endocrine treatment (Makubate et al., 2013). Given the concerns regarding the use of HRT in the majority of breast cancer patients, non-hormonal means for treating hot flushes are needed.

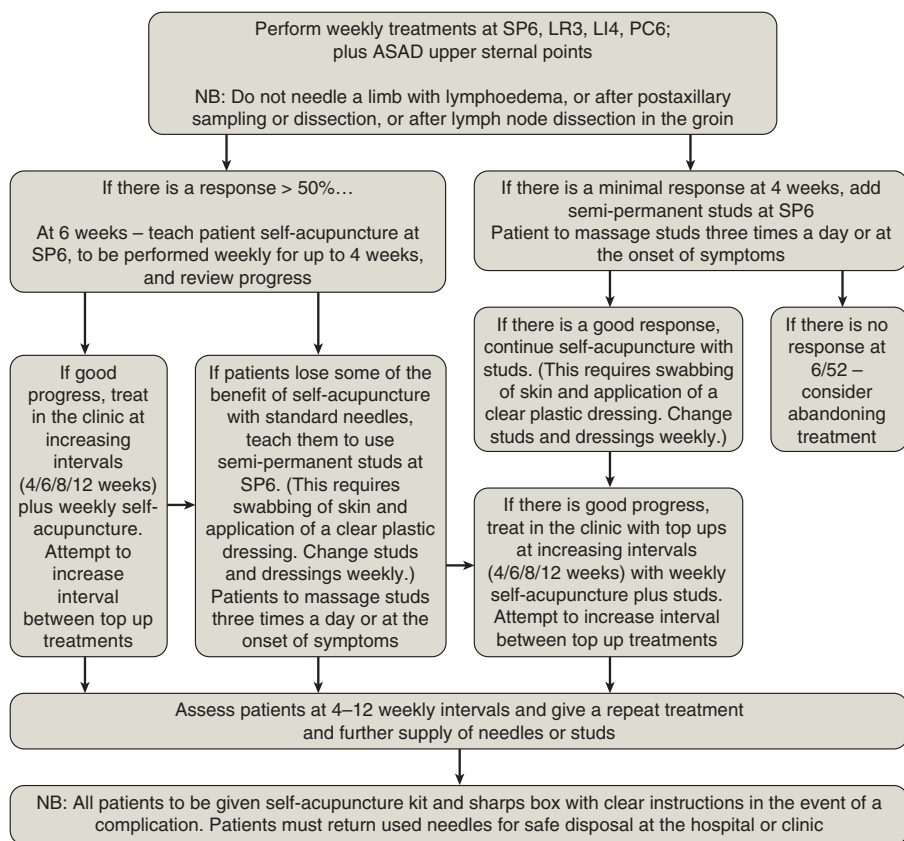
Acupuncture has been used extensively in the United Kingdom for treating hot flushes caused by cancer treatment, and early work has been shown to be effective (de Valois and Jackson, 2003; de Valois et al., 2007; Cumins and Brunt, 2000). Although the exact mechanisms of acupuncture in reducing hot flushes are not certain, it is known that calcitonin gene-related peptide (CGRP) is released into the blood stream during a hot flush and also that acupuncture releases  $\beta$ -endorphin which inhibits CGRP. An RCT looking at hot flushes in the natural menopause showed acupuncture to be effective in reducing hot flushes, and this was associated with a concurrent reduction in CGRP during the treatment (Wyon et al., 1995). Symptoms of hot flushes may also be reduced by increasing  $\beta$ -endorphin levels which have a negative effect on luteinizing hormone surges (Filshie et al., 2005). It has also been shown that stress as well as a reduction in oestrogen and serotonin concentrations can lead to an increase in 5-HT<sub>2A</sub> receptors in the hypothalamus which alter temperature regulation and cause symptoms of hot flushes and sweating (Berendsen, 2000). Acupuncture is known to increase 5-HT (Han and Terenius, 1982) and so may reverse these effects and could also be considered to be the non-drug equivalent of treatment with selective serotonin reuptake inhibitors (SSRIs).

In an audit of acupuncture and self-acupuncture for long term treatment of vasomotor symptoms in 194 cancer patients, 79% showed a reduction of 50% or greater in frequency and/or intensity of the hot flushes (Filshie et al., 2005). This difference makes the symptoms much more acceptable to patients as well as reducing feelings of tiredness. In an early case series of 22 consecutive patients with breast cancer, all claimed some benefit from acupuncture for their hot flushes, and 82% had effective relief (Tukmachi, 2000). One RCT of 50 patients found acupuncture to be as effective as venlafaxine for treating vasomotor symptoms, and there were no side effects in the acupuncture group (Walker et al., 2010). A number of other small randomised trials of acupuncture have demonstrated a reduction in hot flushes in women with breast cancer (Deng et al., 2007; Frisk et al., 2008; Hervik and Mjåland, 2009; Nedstrand et al., 2005). Lee et al. (2009a) reviewed the evidence in patients with breast cancer, and meta-analysis suggested favourable effects compared with sham. Yet they concluded that the evidence was not convincing. Various pilot and other studies in men who had prostate cancer have shown decreases in the frequency and severity of hot flushes (Hammar et al., 1999; Hayes et al., 2005; Frisk et al., 2009; Ashamalla et al., 2011). Yet Lee et al. (2009b) found insufficient evidence to recommend firm conclusions.

Towlerton and Filshie showed that using indwelling semi-permanent acupuncture studs inserted at SP6 on 12 women with breast cancer receiving tamoxifen treatment could help with daily massaging in resistant cases to help maintain the effect (Towlerton et al., 1999). Self-needling with semi-permanent studs was used extensively as a result of these initial findings (Filshie et al., 2005).

It has been noted by one of the authors (JF) that it can take up to 6 weekly treatments for patients to respond to acupuncture for this symptom, which could be regarded as a 'loading dose'; and that breaks in the initial treatment schedule can reduce the effect. An algorithm has been developed for practitioners treating patients with hot flushes related to cancer treatment (Filshie et al., 2005) (Fig. 34.4).

The effects of the initial 6-week course were maintained for up to 6 years (Filshie et al., 2005) and up to 10 years (J. Filshie, personal observation) by using weekly self-needling at SP6 and/or



**Figure 34.4** Algorithm for long term treatment with acupuncture and self-acupuncture.

LR3 or by using semi-permanent needles at SP6 (Fig. 34.5). Self-needling offers patients a flexible approach depending on their lifestyle for up to 10 years which has clinical relevance if tamoxifen, for example, needs to be taken for 10 years. Furthermore It can also be empowering for patients who like a sense of control over their symptoms. It can enable highly symptomatic patients to be compliant with their hormone treatment which would improve adherence over time and ultimately their prognosis. It is essential that clear instructions are given to patients for safe use and disposal of the needles. This is discussed in more detail in the safety section of this chapter.

### Clinical approach

Six weekly treatments using LI4, TE5, ST36, SP6, LR3 and/or ASAD. NB Avoid needling limb postaxillary dissection or axillary sampling. The usual schedule is 6 weekly treatments and then top ups at increasing intervals as shown in the Figure 34.4.

### DRY MOUTH

More than 70% of severely ill cancer patients suffer from dry mouth or xerostomia. It is a distressing symptom which may be caused by medication such as opioids, anticholinergic drugs or antihistamines or previous radiotherapy for head and neck cancer (where the incidence is up to 100%). It may also be caused by the dehydration associated with reduced fluid intake and mouth



**Figure 34.5** Indwelling needles at SP6 and self-administered 'one off' needling sites at SP6 and LR3.

breathing associated with the end of life. It is often accompanied by loss of taste and difficulty in speaking and swallowing. Treatment is usually symptomatic including regular mouth care and the use of saliva supplements rather than addressing the underlying cause of decreased salivary flow.

Several studies have shown the efficacy of acupuncture for xerostomia due to a variety of causes (Blom et al., 1992; Blom et al., 1996) and due to radiation (Wong et al., 2003; Braga et al., 2011; Johnstone et al., 2002b; Garcia et al., 2009). In an RCT of 38 patients Blom et al. (1996) showed increased salivary flow rates in two acupuncture groups, one treated with classical acupuncture and the other with superficial acupuncture so the superficial group was not inactive. In another study of 20 palliative care patients, improvement was seen in visual analogue scores for mouth dryness,

speech and swallowing after 10 treatments (Rydholm and Strang, 1999). A form of TENS (the Codetron) has also been shown to be effective for xerostomia by Wong et al. (2003). Benefit for acupuncture has even been seen in patients with pilocarpine-resistant xerostomia after radiotherapy for head and neck cancer (Johnstone et al., 2001).

One systematic review on the use of acupuncture for xerostomia concluded that limited evidence suggested that acupuncture was beneficial for irradiation-induced xerostomia, and more evidence was recommended (O'Sullivan and Higginson, 2010).

### Clinical points

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Preliminary evidence suggests acupuncture is an effective treatment for xerostomia from different causes.

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While many studies have found high numbers of treatments are needed for xerostomia, in practice when local points are included on the face, six initial consecutive treatments can give significant benefit (J. Filshie, personal observation). Although acupuncture treatment does not prevent the oral sequelae of radiation completely, it has significantly minimised the severity of radiation-induced xerostomia (Braga et al., 2011). One multicentre study compared group acupuncture with group sessions of oral care education. It found a significant reduction in patients' reporting of severe dry mouth symptoms in the acupuncture group compared to oral care. There were also significant reductions in sticky saliva, needing to sip fluids to swallow food and waking in the night to drink in the acupuncture group (Simcock et al., 2013).

There is accumulating evidence for the effect of acupuncture in control of xerostomia during radiotherapy. An RCT ( $n=86$ ) compared acupuncture with standard care and found significant reduction in xerostomia scores and improvement in salivary flow rates in the acupuncture group (Meng et al., 2011). Interestingly the same group did a pilot study ( $n=23$ ) comparing acupuncture with sham acupuncture and no clinical difference was seen in the symptom scores and salivary flow rates between the two groups (Meng et al., 2012). However, this may at least partly be explained by the fact that the sham acupuncture, involved real needling at four ear points which could have had a clinical effect. These studies illustrate well the common problem with acupuncture research where a sham group is used and is assumed to be inactive when in fact the generalised effects of acupuncture may not have been taken into account. Perhaps a useful role for acupuncture in the future could be as a preventative therapy in the management of mucositis in patients with head and neck cancer undergoing radiotherapy.

The possible mechanisms by which acupuncture is thought to improve xerostomia have been outlined by Lundeberg (Lundeberg, 1999). These include release of CGRP a vasodilator which increases salivary secretion. Also, acupuncture has also been shown to increase the release of vaso-active intestinal polypeptide in the saliva of xerostomia sufferers (Dawidson et al., 1998).

### Clinical approach

Local points on face, e.g. ST2 LI20, with auricular points in the region to stimulate parasympathetic control, e.g. Shenmen and lung area. Parasympathetic stimulation is known to increase the volume of saliva. PC6 stimulates parasympathetic activity so is very useful for this indication. Paravertebral points C7–T2 plus trigger points bilaterally. The usual schedule is six weekly treatments then monthly top ups until a plateau in response is reached.

### ANXIETY AND DEPRESSION

Acupuncture like other complementary therapies is often used to relieve anxiety. The 'ASAD' points in the upper sternum are used in numerous cancer centres throughout the United Kingdom to help with symptoms of anxiety and breathlessness. By gently massaging the studs for 1–2 min patients are

able to control these troublesome feelings themselves and induce feelings of relaxation on demand (Filshie and Thompson, 2009). In studies of patients with cancer-related breathlessness, acupuncture including LI4 and ASAD points led to a significant reduction in visual analogue scores for anxiety and improved relaxation following treatment (Filshie et al., 1996; O'Brien et al., 2015). These benefits were prolonged using semi-permanent indwelling needles left in place in the upper sternum for up to 4 weeks at a time and covered by a clear plastic dressing as for breathlessness. A small RCT looking at massage and acupuncture in postoperative cancer patients who were also receiving usual care showed a significant improvement in their depressed mood and a short-lived reduction in anxiety and tension compared to those receiving usual care alone (Mehling et al., 2007).

Acupuncture is often also purported to help with depression; see Chapter 25 (Mental health). These benefits have been backed up by a positive systematic review although most studies were of low quality (Mukaino et al., 2005). A more recent systematic review found the evidence to be inconclusive despite the odds ratio of existing literature suggesting a role for acupuncture (Leo and Ligot, 2007).

## FATIGUE

Fatigue is a common problem in advanced cancer as well as those nearing the end of life with non-cancer diagnoses. It can be exacerbated by treatments such as chemotherapy and radiotherapy and may be helped by drug treatments such as corticosteroids and progestogens as well as lifestyle changes. Non-drug interventions such as exercise and psychological interventions have shown modest benefits. Fatigue is one of the most common and distressing adverse effects of cancer treatment with up to 99% of patients experience some level of fatigue (Servaes et al., 2002). Until recently there has been a gap in the literature in the investigation of the use of acupuncture in treating cancer-related fatigue. In a small study by Vickers et al. (2004) acupuncture reduced the subjective scores for postchemotherapy fatigue in 31% of patients. Another small RCT of 47 patients with moderate to severe fatigue compared acupuncture to sham acupuncture or acupressure, and significant improvements were seen in fatigue levels in the acupuncture group over and above the other two groups; this effect was maintained at 2 weeks (Molassiotis et al., 2007).

In a large multicentre RCT, 302 patients with breast cancer and moderate to severe fatigue following chemotherapy were randomised to receive acupuncture plus enhanced usual care or enhanced usual care alone. Acupuncture given weekly for 6 weeks led to significant improvements in general fatigue compared with the control arm at 6 weeks (Molassiotis et al., 2012). The patients were rerandomised at 6 weeks to practitioner administered top ups or self-needling top ups at ST36 and SP6 versus no further acupuncture. Results were sustained at 10 weeks with a trend toward significance in both acupuncture treatment groups versus no treatment (Molassiotis et al., 2013).

Given the growing body of evidence now available for the use of acupuncture in reducing cancer-related fatigue, self-treatment (usually at SP6 and ST36) can be taught to give long term help for patients. This helps to give a degree of autonomy greatly desired by cancer patients and has cost saving appeal as less follow-up appointments and treatments are necessary.

## Clinical approach

ST36, SP6, LI4 bilaterally (avoiding LI4 on the side of axillary surgery). Six weekly treatment with further top ups using self-treatment at ST36 and SP6 for maintenance as required.

## VASCULAR PROBLEMS

Case reports of radionecrotic ulcers (which classically never heal) have shown complete resolution of the ulcers with repeated acupuncture treatments (Filshie, 1988). The mechanism is thought to be mediated by a degree of sympathetic blockade causing local vasodilation together with local

trophic factors which further improve blood flow. Ischaemic skin flaps and chronic venous ulcers have also been helped by acupuncture including those with breast cancer (Lundeberg, 1999).

### Clinical approach

The main approach involves the use of a surrounding technique, 'surround the dragon', with needles being inserted wide of any hyperaemic area. Additionally '*sympathetic blocking points*' are routinely used: for head and neck and upper limb, use T1 T2 (and possibly C7) paravertebral points, and for lower limb and abdomen add *sympathetic blocking points* L1 + L2. For rectal ulceration add sacral points S2, S3 ± points widely surrounding the ulcerated area, a short distance from it. Six to twelve weekly treatments are needed for ulcers initially, 12 are often needed if ulcers are longstanding or for radionecrotic ulcers in the rectum (personal observation). These can be followed by monthly top-up treatments initially.

### AIDS

AIDS has become a chronic disease for those with access to treatment. Unfortunately despite improvements in survival rates for the disease, the side effects of the cumbersome treatment regimens can greatly adversely affect quality of life. There is accumulating evidence that acupuncture may be beneficial in helping to alleviate some of the side effects of highly active antiretroviral therapy. Gastrointestinal toxicity is one of the main reasons for medication discontinuation. In one study acupuncture decreased gastrointestinal symptoms associated with antiretroviral drugs when combined with relaxation (Chang and Sommers, 2011).

There have been few trials on the use of acupuncture in AIDS. Acupuncture has been found to improve sleep activity and sleep quality following 5 weeks of individualised acupuncture delivered in a group setting (Phillips and Skelton, 2001), however, it not been found to be effective for HIV-related peripheral neuropathy (Shlay et al., 1998). More research into the potentially beneficial effects of acupuncture would be desirable.

### IMMUNOLOGY

In Traditional Chinese Medicine certain acupuncture points are thought to have an influence on immunity. Scientific research in the West has provided limited evidence from experimental animal studies regarding possible immune-enhancing effects of acupuncture (see Chapter 3) but further study is required (Lundeberg, 1999). The mechanisms by which acupuncture, may modulate the immune system is thought to be similar to that of moderate exercise in which increased killer T cell activity has been found (Jonsdottir, 1999).

A systematic review by Lu et al. (2007) in which patients received daily acupuncture for an average of 16 sessions was positive for increasing white blood cells in patients undergoing chemotherapy. However, the quality of the trials included was considered to be poor leading the authors to suggest that the positive meta-analysis should be considered as being exploratory.

### Safety

The risk of significant adverse effects of acupuncture has been shown in a cumulative review by White (White, 2004) to be very low worldwide. He notes that the incidence of significant adverse effects is below that of many common medical treatments, and many of these are likely to be avoidable in the hands of a fully qualified practitioner. Other large prospective studies have also shown acupuncture to have a good safety record (White et al., 2001; MacPherson et al., 2001; Witt et al., 2009). However, there are a number of safety aspects to consider in any acupuncture treatment (see Chapter 14 for full discussion) as well as some specific to palliative care.

Safety is of paramount importance in cancer patients as they appear to be particularly susceptible to the effects of acupuncture, often have complicated disease and the effects of acupuncture may indeed mask underlying disease progression (Filshie, 2001). A good grounding in oncology is important when treating this group with acupuncture. Nursing or other assistance should ideally be available during a patient's first acupuncture treatment, and it is important that a patient is not left alone throughout their first treatment in case of any unusual sensitivity. It is important not to needle too deeply in cachectic patients, in whom a superficial approach should be always be used when needling over the chest wall, lower neck or upper shoulder area to reduce the risk of pneumothorax in these patients.

An absolute contraindication for the use of acupuncture is patients who have severe clotting disorders or who bruise spontaneously. It is also important to avoid needling in the area of an unstable spine due to primary or metastatic bone disease. This is because there is a theoretical risk that acupuncture could precipitate cord compression by removing the protective muscle spasm around the unstable area (Filshie, 1990). Indwelling needles should not be used in patients who are immunocompromised or who have valvular heart disease due to the risks of infection (septicaemia and bacterial endocarditis). Guidelines have been published for the safe use of acupuncture in cancer patients outlining further important cautions and contraindications (Filshie and Hester, 2006).

There are a number of areas where needling should be avoided altogether in patients with cancer. These include over a prosthesis to reduce risk of inadvertent puncture or damage, areas of skin directly affected by metastatic disease or ulceration in order to reduce risk of spreading the tumour. One should also avoid needling limbs where lymph node dissection such as axillary dissection and axillary sampling have been performed to reduce risk the theoretical risk of lymphoedema. Ipsilateral paravertebral needling can help symptoms of lymphoedema in a number of cases but avoid needling the ipsilateral limb directly. While Cassileth et al. (2013) have advocated acupuncture treatment to the limb of patients with lymphoedema, the numbers were small and the authors of this chapter currently advise against needling a lymphoedematous limb, in case of cellulitis occurring in that limb, post-treatment. Paravertebral needling is, however, not contraindicated for this symptom and for lymphoedema of the breast and can be helpful (J. Filshie, personal observation).

Finally it is particularly important in palliative care patients to keep in mind the patients' expectations of their acupuncture treatment which is given for symptom control only and not to give any hint of false reassurance that you are in any way curing their disease. Caution should also be exercised with patients who wish to abandon their conventional treatment in favour of complementary and unproven alternative therapies and those having difficulty coming to terms with their diagnosis who may need expert psychological help.

## Concluding comments

Acupuncture has an increasing role in cancer pain and symptom control. It can be used for a wide range of symptoms in the palliative care setting and as a non-drug treatment it is increasingly popular with patients. There is a growing body of research suggesting that acupuncture modulates neurological processes to bring about its effects, and this is supported by an increasing number of positive clinical studies of varying quality. There is a relative paucity of RCTs, but the evidence that is available is of improving quality with many positive outcomes.

When one considers the numerous side effects of drugs taken by patients, acupuncture has minimal side effects and is generally considered safe when practiced by appropriately trained practitioners. Acupuncture provides an alternative to conventional treatments that is generally acceptable to patients and supportive to them on their often difficult journeys. Acupuncture is increasingly available in hospices throughout the United Kingdom although general awareness of

specific types of evidence supporting its use is very low (Leng, 2013). How to provide such services on an ongoing basis remains a challenge in the United Kingdom and may be best provided in the primary care setting. Acupuncture is a promising alternative to conventional treatment for multiple symptoms in cancer patients, and the authors are optimistic that this challenge will be met in the forthcoming years.

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# Acupuncture in rheumatology

L. Williamson

## CHAPTER OUTLINE

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## Introduction

The speciality of rheumatology encompasses diseases that vary from the most serious and potentially fatal, such as progressive diffuse systemic sclerosis, vasculitis and systemic lupus erythematosus, through to troublesome soft tissue rheumatism complaints.

Clinicians need to be aware that significant systemic illness can present with musculoskeletal symptoms of pain, stiffness or joint swelling. It is therefore important that a full history and examination are taken, and ideally a diagnosis made before patients presenting with musculoskeletal complaints are considered for acupuncture. As it is often not possible to make a definitive diagnosis at onset of symptoms, it is important to exclude red flag symptoms and signs before offering a trial of acupuncture and reassessing early if there is no effect or a short duration effect.

Major advances in the treatment of inflammatory arthritis, crystal arthritis, and osteoporosis mean that conditions that were previously considered chronic and incurable can be effectively controlled, especially if treated early. However, there is still a considerable disease burden carried by patients who have long-standing disease or do not respond to drug therapies.

International agreement on classification of different clinical conditions has meant that national and international clinical trial collaborations have achieved high quality research to answer important clinical questions, for example, in the treatment of childhood arthritis (Juvenile Idiopathic Arthritis, [Petty et al., 2004](#)) and rheumatoid arthritis (RA). In the case of RA, the classification criteria have been updated to identify patients with early disease (6 weeks) and thus initiate effective treatment (ACR/EULAR [Aletaha et al., 2010](#)).

Vickers et al. (2012) published the results of an international acupuncture trialists' collaboration which reported on raw data from 29 good quality clinical trials on acupuncture in chronic pain. The results demonstrate acupuncture as superior to sham and no acupuncture controls in back and neck pain, osteoarthritis and chronic headache. The difficulties in producing good quality clinical acupuncture research cannot be underestimated, and future clinical acupuncture research will be best served by such national and international collaborations.

Funding for treatments will follow good quality evidence of effectiveness and cost-effectiveness. Non-drug therapies such as acupuncture have been included in the treatment guidelines for low back pain (NICE, 2009) following evidence of their effectiveness and recognition of the side-effects of drug therapies, such as non-steroidal anti-inflammatory drugs (NSAIDs) and the limitations of surgery.

Hitherto acceptance of acupuncture has been limited by the lack of biological explanations for relevant effects in clinical practice, whilst experimental research has clearly demonstrated mechanisms for short-term effects (see Neurophysiology, Chapter 3). Neuro-imaging technologies, particularly functional magnetic resonance imaging (fMRI) are being used to explore underlying mechanisms for acupuncture-induced analgesia and other acupuncture effects (see Chapter 4). Exciting early work studying single acupuncture points (Deng et al., 2008), meridian versus segmental points (Zhang et al., 2004), responses to acupressure versus needle and electroacupuncture stimuli (Witzel et al., 2011) and psycho-physical effects during and after acupuncture (Feng et al., 2011) and placebo (Kong et al., 2006) may lead to greater understanding of the underlying mechanisms, and wider acceptance of acupuncture.

## Indications for treatment

The scope for the use of acupuncture in rheumatic diseases is wide (Box 35.1), and there is considerable overlap with patients from general practice, sports medicine, orthopaedics, physiotherapy and pain clinics. Acupuncture is essentially a treatment for symptoms, not diseases, and must be practised in the context of the best medical practice. It is important to exclude possible sinister pathology (e.g. 'red flag' signs in back pain) and ensure that patients are not denied the opportunity of timely drug intervention, for example with RA. It is also important to take a psycho-social history from patients to explore their mood, thoughts, support networks and also areas of secondary gain from their illness in terms of their home relationships, compensation claims or incapacity benefits. These factors all influence illness behaviours and response to treatment.

Treatment strategies presented in this chapter are based on a combination of published evidence, expert opinion and clinical practice.

## Side-effects and disadvantages of acupuncture

Acupuncture is generally a safe treatment but needs to be administered within a strict code of conduct. The commonest side-effects are from needling, namely pain, bruising and vaso-vagal attacks. Bleeding into the soft tissue can lead to swelling, stiffness and worsening of overall pain which may interrupt a rehabilitation programme.

Special care needs to be taken in patients on immunosuppressant medication when needling near or into joints. Some acupuncture points, for example, the Xiyang points, needle into the knee joint. There is a small risk of bleeding into the joint, which in turn might cause an inflammatory reaction and act as a nidus for infection, or cause infection by direct inoculation. For this reason, it is recommended that these and other peri-articular points are not needled in the classical fashion, but superficially and obliquely so that the needle tip touches the outer aspect of the joint capsule only.

**BOX 35.1 ■ Potential applications of acupuncture for musculoskeletal diseases**

Acute pain such as muscle strains and spasm, back or neck pain are often self-limiting; however, simple trigger point or tender point acupuncture can give rapid symptom relief (Camp, 1992) and may prevent development of chronic pain.

Chronic pain and stiffness of shoulders, knees and the low back and neck (Furlan et al., 2005; Vickers et al., 2012).

Adjunctive therapy to drug treatments (Mavrommatis et al., 2012; Vas et al., 2004).

Adjunctive to physical therapies, particularly exercise and physiotherapy (Foster et al., 2007; Soni et al., 2012; Vas et al., 2008).

Perioperative: preop pain relief, waiting list studies for pain relief (Williamson et al., 2007); and aid postoperative rehabilitation (Grotle et al., 2010).

Patient comfort during other painful treatments such as multiple or painful joint injections by relaxation and mild sedation (LR3 point). Anti-emetic (PC6 point) for MTX or cyclophosphamide-induced nausea.

Reduce the overall burden of symptoms in painful conditions by improving muscle tension, sleep pattern, depression (Macpherson et al., 2013), anxiety (Pilkington et al., 2007) and restlessness.

Improve symptoms associated with musculoskeletal disorders possibly including autonomic symptoms, such as coldness, cramps, anxiety, frequency of micturition, irritable bowel symptoms, palpitations.

Improve general well-being. Acupuncture is used by some athletes to enhance performance and some patients to help with fatigue symptoms (Dhillon, 2008).

Chronic pain syndromes. Acupuncture is used to treat chronic pain and may act to counter central pain sensitisation via enhanced descending inhibition, suppressing activated spinal microglia. This in turn may lead to cortical remodelling. These effects have been studied using fMRI in carpal tunnel syndrome (Napadow et al., 2007a,b).

Treatments can be associated with temporary sleepiness and a feeling of general well-being and increased mobility. Rebound pain and fatigue can be difficult to accept unless patients are warned in advance.

## Clinical approach

There are no universally accepted or correct modes of treatment for the use of acupuncture in rheumatological patients. At different times particular types of treatment and forms of needling may be necessary. Evidence from published literature, expert opinion, personal experience and practical considerations will all affect the type and duration of treatment. In general, initial treatments use gentle needling of short duration. Therapy is escalated in duration and intensity according to clinical response, using electroacupuncture if necessary.

A careful history of pain and associated symptoms such as fatigue, anxiety, migraine headaches, irritable bowel or bladder symptoms may indicate whether or not classical Chinese acupuncture points should be used or whether a simple anatomical approach is all that is necessary.

Examine for tender areas such as the tendon ends (entheses), joint margins, osteophytes, tender points or trigger points in muscles and areas of spasm or hyperalgesia in the skin. Muscle spasm may cause muscle shortening which may be identified by asymmetry in the neck and spine, contractures or joint deformity.

Many of the classical acupuncture points, such as those along the Bladder meridian and around the knee and hip joints, are exquisitely tender in rheumatological disorders. Some classical peripheral and central acupuncture points can be used in common rheumatological disorders for their known effects on pain. These are: LR3, SI3, LI4, 9 and 11, BL25, 27, 54 and 57, GB20 and 21 and ST36 (Box 35.2).

**BOX 35.2 ■ Acupuncture points commonly used for the musculoskeletal system****Key points**

LI4, LR3, SP9, SP10, GB30, ST36, LR11, SI3, GB20, GB21, BL54, BL57

**Conditions**

Calf muscle cramps – BL57

Hypertonic muscle – motor point of relevant muscle – teach stretching

‘Sciatica’ – diagnose first – is it myofascial or nerve root? Which is the dominant root?

**Selection from**

BL50, BL52, BL54, BL57, BL60, BL25, BL27

SP9, SP10, GB30

Sacral flats

SP6

**BOX 35.3 ■ Needling regimes used in musculoskeletal disease**

**Classical:** The traditional approach where the aim is to elicit needling sensation (*de qi*). The depth and slope of the needle will depend upon the area and associated structures. The needles are usually left in for 5–20 min.

**Superficial:** The needles are flicked under the skin and either withdrawn almost immediately or left for only a minute or two. This technique may be described as superficial dry needling (superficial needling [Chapter 9](#)).

**Deep, intramuscular:** used for trigger point therapy and often described as deep dry needling ([Dommerholt and Fernández-de-las-Peñas, 2013](#)).

**Periosteal pecking:** the aim is to reach the periosteal plexus of nerves and stimulate them repeatedly for approximately 10 s. This is mainly useful over bony prominences or osteophytes ([Mann, 2000](#)).

**Ear acupuncture:** especially where pain is associated with autonomic symptoms. Useful points are: *Shenmen*, cervical, thoracic and hip, knee and lumbar areas, the eye point and ACTH point.

**Acupressure:** myofascial trigger points can sometimes be treated using firm pressure over trigger points for approximately 30 s. Patients can be taught to treat themselves using this technique.

Standard 25, 30 or 40 mm needles are sufficient for most patients, although occasionally longer needles may be necessary particularly around the buttock area. Needling may be very superficial, deep into muscle, periosteal, or actually into the joint space (though this is rarely performed now in contemporary practice in the West). Clean technique should be used with all needling, and we do not recommend needling into a joint space because of the risk of infection discussed earlier.

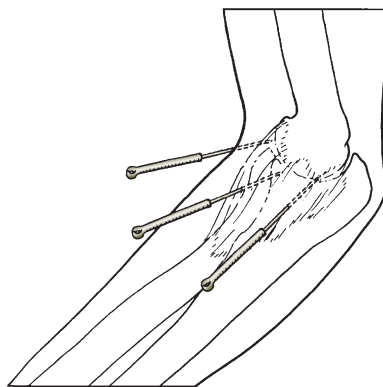
Non-needle techniques such as acupressure and ‘Acu-pens’ devices can be useful for teaching patients to self-treat and for needle-phobic patients, or where needles are contraindicated such as patients with undiagnosed bleeding disorder.

The different needling regimes used in musculoskeletal disease are shown in [Box 35.3](#).

Three particular techniques, described below, may be of special use for musculoskeletal conditions: ‘fanning’ techniques for needling of tendon ends; using fine subcutaneous needles along the passage of nerves and ‘surrounding the dragon’.

The needling of tendon ends by ‘fanning’ is an extension of periosteal pecking ([Fig. 35.1](#)).

The needle is inserted 1–2 cm away from the tendon end and is advanced to tap the periosteum. It is then moved in different directions around the full extent of the insertion of the tendon and at the end of each movement the periosteum should be touched. This technique is uncomfortable and can lead to bruising but may be successful as a substitute



**Figure 35.1** 'Fanning' technique for the treatment of tendinitis.

for corticosteroid injections. The technique can be used for lateral epicondylitis, calcaneal spurs, bicipital tendonitis, Achilles tendinosis and enthesopathies associated with seronegative arthritides. It has been used to treat chondromalacia patellae, where the needles are inserted into the quadriceps muscle just above the patella.

The insertion of the subcutaneous needles above or along the course of a nerve has long been used by the Chinese for acupuncture analgesia (Fig. 35.2). It has also been used in childbirth. The placing of a TENS machine over the sacral nerves during labour mimics this form of acupuncture without the use of needles. This may be used for bladder symptoms as well as low back pain. The technique consists of the insertion of a needle usually over the point of exit of the nerve from the spinal column. In the sacral area, the needle can be inserted just above the third or fourth sacral foramen and then placed so as to lie subsequently above the first to third sacral foramina. Electrical stimulation can if necessary be applied through the needles.

The technique known as 'surrounding the dragon' has been used particularly over denervated or partially denervated areas such as operation scars and in herpes zoster (Fig. 35.3). Needles are placed in a circular fashion, fairly superficially, around the edge or just beyond the area of denervation. They may be stimulated electrically or a TENS machine placed with electrodes on either side of a painful scar.

## TREATMENT SCHEDULES

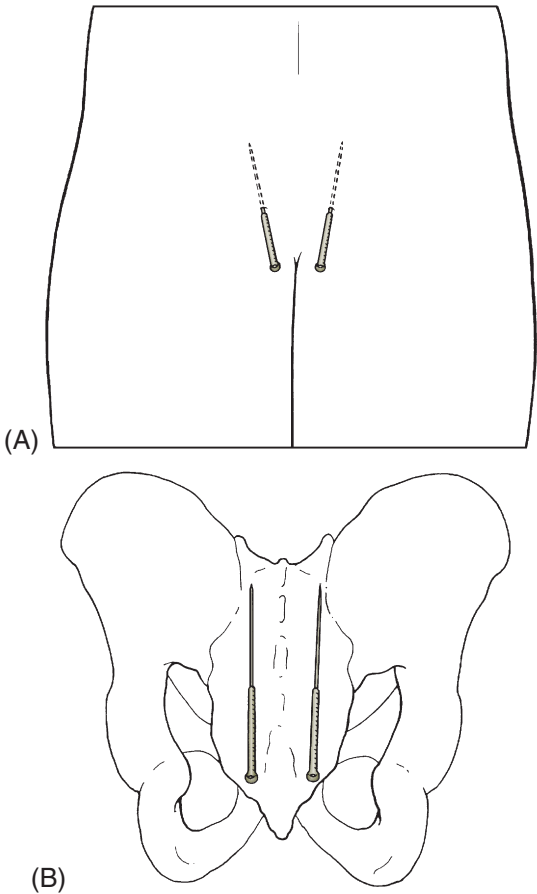
An individual treatment can last anything from 5 to 20 min depending upon the patient, the type of condition and the response to previous treatments. Treatments are initially once or twice weekly and the interval between treatments increased according to effect. Six treatments are often needed before a sustained effect is achieved. Patients often need top-up treatments or repeat courses after 6–12 weeks. If no improvement is seen after 10 sessions, then the treatment should be abandoned.

The importance of stretching, strengthening and general fitness needs to be emphasised, and patients should be encouraged to build up muscle to reduce the likelihood of symptom recurrence.

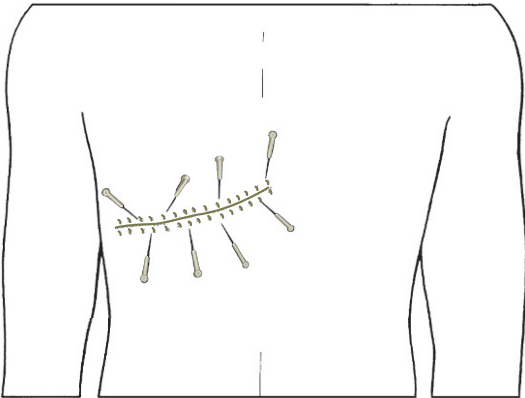
Low dose tricyclic antidepressant and some antiepileptic drugs can act as pain modulators and enhance response to acupuncture (Rafael et al., 2012).

## EVALUATION

It is important to make regular evaluation of the acupuncture response. Patient-reported outcome measures are the most relevant to individual patients. For example, establishing activities they wish to perform, like returning to sport or playing with grandchildren, will help patients understand



**Figure 35.2** A and B: technique of subcutaneous needling: application of ‘sacral flats’ for back pain, bladder problems and autonomic symptoms in the lower limbs.



**Figure 35.3** ‘Surrounding the dragon’ technique for the treatment of postherpetic neuralgia.

treatment effects. Disease-specific outcome measures, visual analogue scales, scales of well-being, scales of night pain and analgesic counts, and the short form McGill pain questionnaire (Collier et al., 1995; Melzack, 1987) can be used for evaluation, audit and accountability.

## PSYCHOLOGICAL FACTORS AND PATIENT PREFERENCE

Psychological factors such as expectations, values, attitudes, personality traits, emotions and social culture affect perception of pain and a person's response to it (Kreitler et al., 1987). Fifty-five percent of acupuncture naive rheumatology patients studied before, during and after a course of acupuncture in an NHS clinic (Collier et al., 1995) responded to acupuncture. There was no difference between responders and non-responders either in their attitudes to or knowledge of acupuncture, but there was a negative correlation between acupuncture response and the trait of anxiety.

Patient expectations and preferences can influence treatment outcomes. In a study of tidal irrigation versus intra-articular corticosteroid injection for knee osteoarthritis, 69% (104 of 150 patients) expressed their preference for treatment at study entry. Patients with a treatment preference who did not receive that treatment had a significant reduction in response compared with those who received their preferred treatment and those with no treatment preference. This data has implications for interpretation of clinical trials results and clinical practice (Thomas et al., 2007).

Understanding the beneficial effects of placebo and the balance between placebo and nocebo effects of treatment is important in interpreting clinical trial results and assessing clinical practice (Zhang et al., 2008).

## TREATMENT FAILURES

Whilst no treatment can be universally successful there are a number of other reasons why acupuncture for the treatment of musculoskeletal conditions may fail. These may include poor case selection, wrong point selection, inadequate treatment duration, poorly controlled or undiagnosed diabetes, and possibly concurrent use of some drugs such as corticosteroids and antipsychotics (or indeed the conditions for which they are used). Patients need to be given realistic expectations of treatment and in the case of chronic pain may accept that a measure of success is functional improvement rather than pain relief.

## CLINICAL APPROACH FOR SPECIFIC CONDITIONS

Soft tissue rheumatism is a term used to describe a heterogeneous collection of conditions with different aetiologies including trauma, overuse, muscle imbalance, tendinopathy and enthesopathies. The success of acupuncture may be increased by examining and treating other parts of the upper limb or related area of the spine. For example, medial and lateral epicondylar pain can be referred from the neck (especially if pain is bilateral), and heel pain may be referred from the back.

### Tendinitis

Acute or chronic tendonitis is traditionally treated by physiotherapy or corticosteroid injections. Acupuncture has been shown to help this condition, at least in the short term (Molsberger and Hille, 1994). The tendon may be treated by direct needling with fanning of the needle from its insertion (see Fig. 35.1), or the area can be treated with EA to local points or segmentally. Trigger points should be actively sought and treated in local and sometimes more distal muscles, for example, forearm extensor muscles in lateral epicondylitis or gastrocnemius and soleus in Achilles tendinosis.

It is important to take an ergonomic history of the cause of the condition. Treatment of trigger points often gives rapid (sometimes temporary) relief of pain and encourages patients to undertake a specific exercise programme to try to prevent recurrence.

It should be remembered that soft tissue rheumatism may be the presenting symptom not only of metabolic diseases such as those of the thyroid and parathyroid glands, but also of the inflammatory arthritides. Sometimes a recalcitrant enthesopathy is the first presentation of reactive arthritis or seronegative inflammatory arthritis such as ankylosing spondylitis (AS), psoriatic arthritis or enteropathic arthritis. A high index of suspicion for systemic disease should be kept where a patient presents more than twice with an acute tendonitis.

## Carpal tunnel syndrome

Carpal tunnel syndrome (CTS) is a common entrapment neuropathy characterised by pain, paraesthesia and sometimes weakness in the median nerve distribution of the median nerve. The spectrum of symptoms varies from mild and intermittent sensory disturbance to severe and persistent chronic pain, associated with irreversible sensory loss and muscle wasting. The aim of treatment is to alleviate symptoms in mild-to-moderate cases and prevent permanent nerve damage in severe cases.

A systematic review of acupuncture and CTS (Sim et al., 2011) included six trials, two with sham and four with active controls, plus a meta-analysis of acupuncture versus corticosteroid block therapy (two studies). It concluded that evidence was encouraging but not conclusive.

More recent studies of acupuncture in mild-to-moderate CTS have shown improvement with acupuncture plus night splinting above sham acupuncture plus Vitamins B1, B6 and night splinting (Khosrawi et al., 2012); no significant difference with acupuncture plus night splinting versus placebo acupuncture (Streitberger needles) plus night splinting (Yao et al., 2012); superiority of EA above night splinting for pain, but not function (Kunnerddee and Kaewtong, 2010); and superiority of EA effect above acupuncture in symptoms, grip strength and electrophysiological function (Ho et al., 2014).

Functional MRI studies of acupuncture in CTS patients are advancing our understanding of chronic neuropathic pain. Napadow et al. (2007a) demonstrated differences in hypothalamic and amygdala responses to acupuncture between CTS patients and healthy controls. CTS patients also showed maladaptive cortical responses which improved with acupuncture, thus demonstrating somatosensory cortical plasticity in response to acupuncture (Napadow et al., 2007b).

## Adverse neural dynamics

This common condition presents with pain, paraesthesiae or numbness in the arms or legs due to restriction or irritation of a nerve anywhere along its course distal from the spine. Symptoms can be provoked or reproduced by neural mobilisation tests (Butler, 2000; Schmid et al., 2009) and in the legs can be provoked by straight-leg raise and 'slump tests'. Symptoms and signs are most commonly associated with poor posture, particularly in those who use computers for long periods. They are often present in work-related upper-limb disorders related to repetitive use or overuse activities, such as excessive keyboard work. They can also present in patients who suffer from whiplash injuries or any inflammatory or mechanical arthritis.

Acupuncture to myofascial trigger points and shortened muscles can be helpful in treating acute pain. Symptoms may return unless patients improve their posture and core strength. Acupuncture is best used in combination with physiotherapy and a graded exercise programme. Cases may be multifaceted and complicated by chronic pain, work disability and compensation claims. Long established cases are often intractable and difficult to treat.

## Shoulder pain

Shoulder pain is common with a lifetime prevalence of 10% according to one survey (van der Heijden, 1999). Patients complain of pain, restricted movement, and loss of function which may be due to intrinsic shoulder disorders, or referred from the neck or thorax. The more common intrinsic shoulder disorders are rotator cuff lesions (65%), pericapsular soft tissue pain, adhesive capsulitis and osteoarthritis (Vecchio et al., 1995). Shoulder pain may be self-limiting, but a 3-year follow-up study found 54% of patients had persistent pain and 90% with disability (Macfarlane et al., 1998) causing reduced quality of life and functional impairment with significant cost to the patient and society. Eighteen percent of reported Swedish disability payments were for neck and shoulder pain (Nygren et al., 1995).

Acupuncture has been compared with placebo, steroid injection, ultrasound, acupuncture plus mobilisation exercises (Green et al., 2005), with limited evidence of short-term benefit of acupuncture compared with placebo. Vas et al. (2008) compared a single point acupuncture technique (through needling from ST38 to BL57) during shoulder mobilisation followed by physiotherapy with mock TENS during shoulder mobilisation followed by physiotherapy alone in a randomised controlled trial of 425 patients with subacromial syndrome. After 4 weeks there was a significantly greater change in Constant-Murley score and decrease in analgesic consumption in the acupuncture group. A randomised, sham-controlled, patient-blinded, multi-centre trial of 424 outpatients with unilateral chronic shoulder pain demonstrated a 65% ( $n=100$ ) improvement in the verum acupuncture group, versus 24% ( $n=32$ ) in the sham group and 37% ( $n=50$ ) with conservative orthopaedic treatment,  $p < 0.01$  (Molsberger et al. GRASP 2010).

Shoulder assessment should always include the neck and thoracic spine. Muscle spasm and trigger points in the trapezius, rhomboids, and levator scapulae muscles can cause elevation of the scapula and painful restriction of shoulder movement. Commonly used points for treating shoulder problems are: LI16, SI913, LI15; TE14; GB34; ST38 and BL57, plus trigger points in the neck, around the shoulder and scapula posteriorly and pectoral muscles anteriorly.

## Osteoarthritis

Osteoarthritis is the most common joint disease worldwide and is a major cause of morbidity and physical limitation particularly in the elderly. As populations age, the problems of osteoarthritis are being compounded by rising obesity and lack of physical activity.

Acupuncture has been shown to help osteoarthritis pain, but it is important that it is seen as one facet of a treatment strategy which will help patients improve physical activity and hence their general health. Indeed without increasing muscle activity and bulk around affected joints the pain is likely to return.

Primary generalised nodal osteoarthritis (PGNOA) occurs most commonly in middle-aged females, often initially affecting the proximal and distal interphalangeal joints of the hand and can be associated with minor stiffness or 'gelling'. PGNOA is considered a polygenic hereditary disorder and patients often develop hip, knee or spinal OA in older age. Whatever the cause of OA, once the condition is established, the most important preventable risk factor for disease progression is obesity (Neogi and Zhang, 2011)

It is important to distinguish OA from early RA, which also commonly affects the same population group, as early RA should be treated with disease modifying anti-rheumatic drugs (DMARDs). The distinction can be difficult as some OA changes can be inflammatory and destructive. In practice, acupuncture is used to extra points between the metacarpophalangeal joints, classical acupuncture points such as L14 point, tender points in the lumbricals and interossei muscles, and along the tendons between the proximal and distal interphalangeal joints. An important challenge for future studies is to better define the role of acupuncture in this common and disabling condition.

*Thumb base pain* is often the first troublesome presentation of OA. Pain may be localised around the thumb base or radiate to the wrist and forearm. Treatment options are limited to analgesics, corticosteroids injection and trapeziectomy for advanced disease.

Patients, particularly those with early disease, respond well to LI4 (plus trigger point and tender point) acupuncture which allows increased thumb abduction. Patients can be taught to press this point themselves and should be encouraged to practice daily stretching exercises to maintain hand function.

## KNEE OSTEOARTHRITIS

The knee joint is one of the most rewarding to treat with acupuncture. RCT and meta-analysis of pooled data have demonstrated effectiveness of acupuncture in mild to severe knee osteoarthritis (Manheimer et al., 2010; Vickers et al., 2012; White et al., 2007).

Questions still remain about what is the best form of acupuncture to use and the optimum treatment strategies either alone or in combination with exercise or physiotherapy regimes. Exercise is a key recommendation of current guidelines for the management of OA, with some evidence in favour of acupuncture for knee OA (NCCCC, 2008). Data from clinical trials about exercise and exercise therapy is inconsistent because studies are heterogeneous in terms of population included, type of acupuncture administered, control groups, outcome measures, timing of follow-up and presentation of data.

### Clinical points

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High quality evidence confirms the effectiveness and cost-effectiveness of acupuncture for treating knee osteoarthritis. Acupuncture is recommended in guidelines.

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Scharf et al. (2006) demonstrated superior effects of acupuncture over exercise, whereas Foster et al. (2007) demonstrated no benefit of combined acupuncture and physiotherapy above physiotherapy alone. This latter study differs from others because the patient group had relatively mild knee OA, EA was not used, and the advice and physiotherapy treatment was probably more intensive than in other trials. Therefore this probably does not represent usual practice, where acupuncture is reserved for those who have not responded to exercise alone.

Evidence supports the role of acupuncture in knee osteoarthritis; it should be used in conjunction with long-term exercise.

Patients with severe OA are often offered knee replacement surgery as the only therapeutic option. Recent data of total knee replacement patients has demonstrated that 20% at 1 year remain dissatisfied after a technically successful procedure (Baker et al., 2007). In waiting list studies of acupuncture for severe knee OA, 20–25% of the acupuncture group patients opted to cancel their surgery for a number of reasons including symptom relief, improved function or preference of acupuncture over risks of surgery (Soni et al., 2012). It would therefore be reasonable to study the suggestion that patients with severe knee OA symptoms have a course physiotherapy plus acupuncture in advance of referral and before expectation for surgery. This might be delivered in an NHS outpatient group setting (Soni et al., 2012) or an extension of the high volume acupuncture clinic (Berkovitz et al., 2008). Acupuncture treatment is recommended in US guidelines for patients who are unable to have surgery (Hochberg et al., 2012).

Some common treatment approaches are summarised in Box 35.4.

Some useful clinical points:

- Always check the hip and spine before starting treatment for knee pain;
- Assess for depression and social isolation, as well as radiological changes, to help understand how best to help patients manage their pain and disability (Ozcakir et al., 2011);
- Knee joint function relies on the strength and integrity of the quadriceps muscles and patients should be strongly encouraged to exercise these in order to maintain any lasting benefit from acupuncture;

**BOX 35.4 ■ Treatment of the knee joint****Acute pain and stiffness**

SP9, SP10, BL54, BL57, ST33, ST36

*Xiyan* – electrical or manual stimulation

**Chronic pain**

SP9, *Xiyan*, BL54, BL57, LR3, LR9, ST33, ST36, SP10

Tender and trigger points

Ear points can be added

*Xiyan* (superficial, to not penetrate joint; avoid pre- and postjoint replacement surgery)

**Anterior knee pain**

Periosteal stimulation of patellar margins

'Fanned' stimulation of patellar attachment

Treat trigger points in adductors, vastus medialis obliquus and tensor fasciae latae muscles

- In retropatellar knee pain (anterior knee pain), targeted vastus medialis obliquus muscle training and often tensor fasciae latae muscle stretching are often used in addition to acupuncture;
- Knee OA is accelerated by obesity;
- Avoid the 'knee eye' points, particularly before or after joint replacement surgery.

**Neck and back pain**

In assessing a patient with back pain it is important to rule out sinister underlying pathology and make a diagnosis if possible. Acupuncture to paraspinal muscles is contraindicated if there is an unstable spine caused by trauma, malignancy or infection because it may reduce protective muscle tone and, theoretically, increase the risk of transection of the spinal cord. Inflammatory back pain from AS is worse on rest and improved by exercise. It is best treated with NSAIDs, physiotherapy and intensive daily exercise and then anti-TNF biologic therapy. There is little published data on the use of acupuncture in AS, but in clinical practice it is helpful for pain and general well-being, particularly in NSAID intolerant patients. Osteoporotic crush fracture can present with sudden onset severe pain. Investigation and treatment is needed to prevent further fracture. Acupuncture is helpful for acute pain relief. Patients with pain which suggests malignancy or new neurological signs and symptoms including saddle anaesthesia, incontinence and spasticity require urgent referral and investigation.

After serious pathology has been excluded, patients should be encouraged to keep as active as possible. The recognition that rest delays recovery and worsens prognosis has improved outcomes for acute back pain. NICE have acknowledged the place of acupuncture and of patient preference in the management of persistent low back pain. Patients can choose between three physical therapies, and this will hopefully maximise improvement, speed recovery and return to work and prevent chronic pain. It will be interesting to evaluate the uptake and effects of these guidelines on the prevention of chronic back pain.

**Clinical points**

Evidence shows that acupuncture is more effective for back pain than both no acupuncture and sham controls and cost effective well below the recognised threshold. Guidelines recommend acupuncture for chronic back pain.

**BOX 35.5 ■ Spinal problems potentially responsive to acupuncture**

Non-specific acute and chronic pain  
 Cervical headache  
 Occipital neuralgia  
 Nerve root pain of arm or leg  
 Fracture pain  
 Malignant pain  
 Arachnoiditis pain  
 Postintervention and other neuralgias  
 Ankylosing spondylitis  
 Osteoarthritic symptoms  
 Osteoporotic fracture pain  
 Discogenic disease  
 Postlaminectomy pain

For patients with existing chronic back pain, acupuncture can be used as part of an overall back management programme which must address patient attitudes, perceived disability, pain behaviour, lack of activity and conditioning, as well as the pain itself ([Melzack and Wall, 1982](#)).

Careful clinical examination will include assessment of gait, muscle bulk, muscle spasm, spinal mobility, neurological status, trigger points, tender points, hyperalgesia and skin temperature changes. The approach to acupuncture involves local, segmental and meridian points.

Spinal problems for which acupuncture is worth a clinical trial are listed in [Box 35.5](#).

## Rheumatoid arthritis

RA (of which the global prevalence is 1%) is an autoimmune condition with considerable morbidity, functional impairment, disability and increased mortality. Major advances in the drug treatment of RA have led to dramatic improvement in outcomes, particularly in early disease. The major contributing factor to this change is the emphasis on early treatment, aggressive drug therapy and the recognition of the ‘window of opportunity’ (within the first 3 months) where effective drug therapy can hope to achieve a clinical remission. However, there is still a considerable disease burden carried by RA patients who do not respond to chemotherapy and those with long-standing disease. In addition, drugs have frequent side-effects and biological therapies are extremely costly. Some are unaffordable in resource poor countries and ‘rationed’ in others. Furthermore there is no data on the long-term effects of biological therapies. The place for non-drug therapies such as acupuncture in RA and inflammatory arthritis is therefore evolving and remains important to study ([Box 35.6](#)). A key question to answer is whether targeted fine needle

**BOX 35.6 ■ Some roles of acupuncture in rheumatoid arthritis**

Reduce local joint pain and muscle stiffness, increase joint mobility  
 Inactivate myofascial trigger and tender points  
 Reduce stress and pain of injections and painful procedures  
 Treat nausea secondary to DMARDs  
 Hand function – treat small muscles of fingers  
 Allow better exercise and minimise muscle loss (sarcopenia)  
 Improve sleep and general well-being  
 Augment relaxation and pain relief during painful procedures such as multiple joint injections

stimulation of the peripheral nervous system can lead to immunomodulatory changes which normalise the immune response in early RA.

Early clinical trials of DMARD therapy in RA were disappointing, demonstrating symptom relief only rather than prevention of long term joint damage. It was the recognition that DMARDs needed to be commenced early in disease, as soon after diagnosis as possible, that has led to improved outcomes. In addition a new International ACR/EULAR classification ([Aletaha et al., 2010](#)) allows for identification of early disease and therefore enables further studies into the treatment of early disease with the ultimate target of effecting drug-free remission. Likewise, studies of acupuncture in RA, which had disappointing results, have been in patients with established disease. This is likely to be too late in the disease process to expect more than palliation of symptoms. A systematic review of acupuncture in RA ([Lee et al., 2008](#)) failed to show any specific effects for pain control. Other studies have demonstrated short term clinical improvement but failed to demonstrate reduction in ESR or CRP, disease-specific outcome measures or regional inflammatory findings on  $^{18}\text{F}$ -FDG – PET scan images ([Sato et al., 2009](#)).

RA patients develop myofascial problems and secondary osteoarthritis, and treatment of myofascial trigger points can be particularly rewarding. Pain may present over a joint but is actually referred from muscle. Common sites include the jaw (masseter and lateral pterygoid muscle), wrist (wrist extensors), hip and greater trochanter (gluteal muscles) and knees (quadriceps femoris).

*Costochondritis* often responds to careful, superficial needling of tender points which can avoid the need for intra-articular corticosteroid injections. *Occipital pain* can be debilitating and neuralgic in quality. This can also respond to superficial needling, if necessary starting on the contralateral side to the pain. Symptoms of early or painful 'swan-neck' deformity and ulnar deviation are sometimes relieved by tender point needling to the interossei and lumbrical small muscles of the hand.

Methotrexate (MTX) is the most widely used DMARD medication, and nausea is a common side-effect which limits dosage and compliance. PC6 acupressure, either manually or using commercial 'sea bands', helps patients with mild MTX-induced nausea.

Intra-articular corticosteroids are successfully used to settle acutely inflamed joints. In early disease and in disease flare, patients sometimes have multiple joint injections, often into the small joints of the hand. Needling a single LR3 point can relax anxious patients in preparation for single or multiple injections. Needling LI4 reduces pain of injections into multiple finger joints, especially into the interphalangeal joints which can be very painful.

Fatigue and depression are common in RA, even in patients whose disease activity is well controlled. A qualitative study of RA patient experience receiving acupuncture from either traditional or Western acupuncturists found that patients perceived an improvement in mood, energy and sleep pattern ([Hughes et al., 2007](#)). In addition the perceptions and affiliation of the acupuncturists led to different patient perceived outcomes. 'Being treated as a whole' by the traditional acupuncturist improved experience and outcomes, whilst perceived lack of time by some NHS patients adversely affected outcomes ([Hughes, 2009](#)).

In addition to composite scores of disease activity (DAS 28, ACR 20 and ACR 50), outcome measures in RA include quality of life measures (EUROQUOL, SF36), function (HAQ), work attendance, presenteeism and patient related outcome measures (PROMs). Disease costs included drugs and treatment, plus costs to patient and society in terms of lost earnings of patients and carers, and benefits claimed. Future clinical trials of acupuncture as adjunctive treatment in RA need to be evaluated in these terms.

## Sjogren's syndrome and sicca symptoms

Sjogren's syndrome is an autoimmune syndrome affecting up to 1% of the population characterised by sicca symptoms of dry eyes, mouth and vagina associated with general fatigue and myalgia. The condition is often under-diagnosed because of the non-specific nature of the symptoms,

which are often overlooked in routine history taking. Severity varies from mildly troublesome sicca symptoms to life-threatening systemic illness.

The prevalence of dry eye in the general population is 11–17%, and secondary Sjogren's symptoms occur in up to 30% of other connective tissue diseases, in particular SLE, RA and scleroderma. Acupuncture has been shown to improve tear break-up time, Schirmer test score and response rates compared with artificial tears in a systematic review of acupuncture studies for Sjogren's and dry eye patients (Lee et al., 2011).

Similarly, acupuncture is also used to treat dry mouth symptoms (xerostomia). Acupuncture has been shown to increase stimulated and unstimulated salivary flow in healthy volunteers (Davidson et al., 1997), primary and secondary Sjogren's syndrome patients (Blom and Lundeberg, 2000) and radiation-induced xerostomia (Johnstone et al., 2001). A study of chronic radiation-induced xerostomia showed group acupuncture provided significantly better relief of symptoms compared with group oral care education, but with no increased salivary flow (Simcock et al., 2013).

An exploratory fMRI study of unilateral manual acupuncture stimulation of the LI2 point (a point on the proximal and radial aspect of the index finger, commonly used in the treatment of xerostomia) showed increased bilateral activation of the insula and adjacent operculum regions of the brain which are associated with gustation/salivation. Non-penetrating sham acupuncture at a non-point site on the ulnar aspect of the wrist induced neither activation nor deactivation of these areas. LI2 acupuncture induced more saliva production than sham acupuncture (Deng et al., 2008).

## **Fibromyalgia, widespread pain and chronic fatigue syndromes**

These diagnoses fall within a spectrum of chronic disorders characterised by widespread musculoskeletal pain, associated with multiple bony tender points, fatigue, morning stiffness and poor sleep pattern. Depression may be a prominent or masked feature. A full biopsychosocial history to identify underlying family dynamics, stressors and triggers and features of secondary gain such as disability and compensation claims need to be clarified before treatment is offered. Treatment should only be given as part of a multidisciplinary team approach with psychological and physiotherapy support. Low dose tricyclic antidepressants given at night, aerobic exercise and cognitive therapy have been shown to be helpful (Häuser et al., 2010). Acupuncture to hypersensitive painful points or traditional points needs to be gentle and rarely has lasting benefit unless an improved sleep pattern is established. Evidence from RCTs seems to favour the use of EA over manual acupuncture, and this might suggest that this group is generally under treated, perhaps because they find strong sensory stimulation painful.

## **Complex regional pain syndrome**

Complex regional pain syndrome (CRPS) (Type 1 – without nerve damage – formerly reflex sympathetic dystrophy; Type II with nerve damage – formerly causalgia – Harden et al., 2007) is a condition affecting a limb characterised by severe pain, swelling and skin changes (oedema, abnormal sweating, colour changes). The limbs become hyperalgesic and allodynic with pain of neuropathic quality, disproportionate to physical signs and unresponsive to drug treatments. The cause is unknown, but precipitating factors include injury (sometimes trivial), immobilisation or surgery, although there is often no clear cause. Patients also display neglect, referred sensations and visuospatial anomalies.

Diagnosis is commonly delayed (mean time to diagnosis is 30 months) with referral to multiple different clinicians. Diagnosis is clinical and by exclusion of other conditions. A significant proportion of patients (20–50%) develop chronic intractable illness, and early recognition and treatment can lead to complete recovery.

Clinical and functional imaging studies (Schwenkreis et al., 2009; Swart et al., 2009) suggest that symptoms are a result of reorganisation in central somatosensory and motor networks, which lead to altered central processing of tactile and nociceptive stimuli, and autonomic nervous system dysregulation. Treatments including mirror therapy (McCabe et al., 2003), tactile discrimination (Moseley et al., 2008) and tactile graded imagery (Moseley et al., 2012) target cortical areas, aiming to restore the impaired sensorimotor function, and have recently shown promising results. Acupuncture may be a very useful treatment modality, particularly for early disease. The affected limbs may be too painful to touch or even approach. In this case the contralateral limb can be treated.

Small studies of acupuncture and CRPS showed improvement in pain in classical acupuncture groups compared with sham acupuncture groups (Fialka et al., 1993), plus an increase in skin temperature in both groups (Kho, 1995). Hommer (2012) reports the successful use of Chinese scalp acupuncture in two US military veterans with recalcitrant upper-limb CRPS, with a sustained treatment response at 20-month follow-up. In clinical practice in early CRPS, acupuncture to contralateral LR3 point together with mirror therapy has been associated with improved limb colour and decreased pain, enough to allow the patient to perform a useful functional task such as touch the limb, wash their hands, wear a shoe or weight bear in a first treatment. Patients with early disease may continue to improve after the first treatment. However, the pain may return rapidly, and patients should be warned about this and plan a course of treatment. Patients with chronic CRPS have a poor prognosis and poor response to any treatment. They require multidisciplinary help including general practitioner, physiotherapy and psychology support.

The key to successful outcome in CRPS is likely to lie in early recognition and diagnosis and treatment. The role of acupuncture in the treatment of this painful and potentially devastating condition needs to be further studied and defined.

## Concluding comments

Acupuncture has an established place in the treatment of non-inflammatory musculoskeletal conditions. Future clinical trials need to address effectiveness, optimum modes of treatment and importance of adjunctive therapies.

In the field of inflammatory arthritis, any immunomodulatory effects of acupuncture, particularly in very early RA, plus effects of adjunctive acupuncture on drug costs, general well-being and function will be important areas to study. Exciting areas of future research include the effects on neural plasticity and cortical reorganisation in the treatment of early CRPS and chronic pain. More difficult research challenges will be to demonstrate whether early treatment prevents chronic disease, with a cost-benefit analysis. The final challenge is how to deliver affordable and effective acupuncture within a limited health budget.

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# Acupuncture in sports medicine

K.V. Trinh ■ S.J. Scott ■ E. Ho ■ L. Field

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## Introduction

Acupuncture is commonly used by physicians or therapists in sports medicine (Pelham et al., 2001) for various reasons. The most common are probably for pain management, functional rehabilitation (Usichenko et al., 2011) and performance enhancement (Dhillon, 2008; Usichenko et al., 2011). For pain management and functional rehabilitation, the most commonly treated conditions are shoulder and knee conditions, accounting for about 70% of the cases the authors encountered in their sports medicine practice. These conditions will be dealt with more extensively after discussion of performance enhancement. Other conditions often encountered, such as lateral epicondylitis, trochanteric bursitis, iliotibial band syndrome and ankle sprain are not further discussed here but can be approached using principles illustrated in the sections on shoulder injury and knee pain.

## Enhancement of sports performance

Acupuncture is also used for performance enhancement in sports, helping athletes to deal with pregame anxiety and postgame relaxation or pain relief and functional improvement during sports participation. Some authors have used the term acupuncture 'doping' to refer to the acupuncture performance enhancement. Taking a prohibited substance is banned in national and international sports, whereas using acupuncture to enhance performance is allowed in national and international all competitions. There is little good research evidence supporting acupuncture in this setting.

There are published articles describing some practitioners' experiences with enhancing performance with acupuncture. Dhillon (2008) described a study with 20 male cyclists to examine the effect of acupuncture on 20 km cycling performance. In this prospective, single-blind study, the

subjects served as their own control. They had 3 tests a week, riding a stationary bike for 20 km as fast as able. Before each test, they received acupuncture, 'sham' acupuncture, or no intervention control, once each in a random order. The following outcomes were measured: time to completion, VAS for lower extremity/exercise-induced pain, Borg rating of perceived exertion (RPE) and blood lactate concentrations. The RPE was significantly different in favour of acupuncture (Dhillon, 2008). The higher RPE scores represent a clinically significant effect considering the reduction in time and VAS measures. This study concluded that acupuncture treatment has the potential to improve the effort exerted by athletes without diminishing performance.

A systematic review by Urroz et al. examined four clinical trials investigating acupuncture treatment as a potential method of improving exercise performance and postexercise recovery. While the results were, as a whole, inconclusive because two of the trials demonstrated significant positive results and two revealed no effect, this systematic review provides preliminary evidence of acupuncture for athletic improvement. The review supports further investigation into this area topic of interest (Urroz et al., 2013).

Usichenko et al. (2011) described a case report of a modern pentathlon athlete. This sport involves swimming, fencing, steeplechase, running and shooting. This athlete was a 20 year old in the former Soviet Union national team. There were several symptoms limiting this athlete's performance, including epigastric pain, knee weakness, wrist pain, arm fatigue, tremor and shoulder stiffness. After the athlete started a programme of acupuncture treatments, his performance improved in the 3000 m cross-country running. His other symptoms were also significantly improved (Usichenko et al., 2011).

The study by Kaada (1984) evaluated the exercise performance of trained athletes. The experimental group used low frequency transcutaneous nerve stimulation prior to activity, and the results consistently demonstrated an improvement in performance compared to the control or placebo groups. The author reported a mean improvement of 2.3 s in 800 m track racing ( $n=5$ ) and 4.3 s in 1000 m road racing ( $n=9$ ). These competitive track-and-field athletes had electrical stimulation of LI4 compared to placebo stimulation.

A small study on 33 recreational athletes in Germany demonstrated the potential of acupuncture in strength training. These athletes had a single acupuncture treatment session and had various outcomes measured. It was found that the group with acupuncture treatment had a significant improvement in their quadriceps isometric strength compared to the sham treatment group (Hübscher et al., 2010).

One of the authors (K. Trinh) has significant experience with international sport competitions. He has treated many high performance athletes with acupuncture. For relaxation before performance, points used before were GV 24.5 and LI4 (stimulated bilaterally manually) for 15 min. The athletes were then left in a dark room for rest after the treatments. Athletes have claimed improvement in performance.

There is little solid research evidence for acupuncture for enhancement of athletic performance. The small studies mentioned and other testimonies may be describing strong placebo effects. Psychological support from the medical team and the spectators may have strong influence in the athlete's performance. Further research in this area will be helpful in determining the effect of acupuncture for sports performance enhancement. However, treating athletes for their musculoskeletal conditions successfully may enhance their functions and thus their performances. We will focus on shoulder and knee conditions, the two most commonly injured areas in sports medicine.

## Shoulder problems

Musculoskeletal shoulder pain is a one of the top three musculoskeletal pain complaints, with a population prevalence of up to 16% in some surveys. It is not limited to particular age groups or

physical activities, but it is more common among athletes (Bigliani and Morrison, 1986; Dinnes and Loveman, 2003; Goldstein, 2004).

The common shoulder problems related to sports injury seen daily in primary care are: rotator cuff pathology, impingement syndrome, instability and labral lesion. For sports like tennis or baseball which involve throwing, overhead positions and the use of a racquet, muscle and tendon injuries are common from overuse and repetition or faulty techniques. Very often, the types of injury range from tendonitis to overuse tear. For swimming, it was reported that up to 40–70% of competitive swimmers complained of shoulder pain. In our clinical experience we see people suffering from impingement who go on to develop tendon pathology and instability. In contrast, in sports with high energy contact and impact, like football or hockey, the common shoulder injuries are related to acute tendon tears or dislocation (Flatlow et al., 1994; McCann and Bigliani, 1994; Matsumoto et al., 2002; Pink and Tibone, 2000; Yanai et al., 2000).

## ROTATOR CUFF PATHOLOGY

In the population whose sports involve repeated overhead positions or throwing manoeuvres, it is very common to see rotator cuff tendon problems. There is no single direct contributing factor to rotator cuff pathology. In order to understand rotator cuff pathology, we have to take a look at the structure of shoulder girdle anatomy and kinetic mechanism. The shoulder girdle including the glenohumeral joint is a complex structure. Shoulder movement depends on the scapular relationship and motion relative to the body as well as range of movement of the glenohumeral joint. The shoulder girdle is responsible for providing both stability and mobility at the same time while we move our arms (Grant, 2004; Kelkar et al., 2001).

The rotator cuff is bounded by a few structures – the coraco-acromial ligament, the coracoid process and the acromion – which together form a solid arch-like structure to allow the rotator cuff tendons to go through. Compression friction force is created by the arch while the arm is in extreme external rotation at 90° shoulder abduction position (e.g. before throwing a ball in baseball or serving a ball in tennis). This manoeuvre will put stress on the tendons (Brown et al., 2000). Furthermore, there are reports suggesting that there is a relationship between cervical neurological problems, suprascapular nerve injuries and rotator cuff pathology (Kaplan and Kernahan, 1984). If there are any cervical neurological problems involved, the possibility of developing rotator cuff pathology is even higher, as there will be possible muscle imbalance which develops excessive compression force. Inadequate rehabilitation care will increase the risk of chronic rotator cuff tendonitis and adhesive capsulitis.

## SUBACROMIAL IMPINGEMENT

Subacromial impingement results from insults to the soft tissue by the skeletal structure around the acromial area, as described in the previous paragraph. While the impingement could be related to overuse, overhead positions and even degenerative changes of the acromial structure, impingement can also result from muscle imbalance which leads to glenohumeral akinesia and scapular malpositioning with poor posture (Budoff and Hammond, 1998; Lukasiewicz et al., 1999). Sports activities involving heavy training in overhead positions or 90° abduction or more also cause the excessive compression of the soft tissue underneath the acromial bony structure (Harryman and Sidles, 1990; Hawkins and Kennedy, 1980).

## GLENOHUMERAL INSTABILITY

The stability of the glenohumeral joint relies heavily on the biomechanics of shoulder muscles and their influence on the two stability mechanisms: glenohumeral alignment and concavity

compression (Matsen, 1994). Poor alignment can change the kinetic motion of the humerus against the glenoid cavity and affect shoulder function (Goldstein, 2004). In addition, the rotator muscles are playing an important role in applying compression force to humerus against the glenoid cavity and allowing concentric muscle work of the prime movers like pectoralis, biceps and deltoid to pull the arm (Howell and Galinati, 1988). Any changes in the rotator cuff muscle power will significantly affect the concavity compression. As the concavity compression is reduced, there will be an increase of anterior translation instability of the humeral head in response to pectoralis and biceps muscle activities. While ageing is one of the reasons for the change of vascular supply to the rotator tendon that could lead to tendinopathy or a tear, there are also studies suggesting that neurological injury can lead to shoulder instability or even dislocation (Grob, 1995; Rodosky et al., 1994).

## SUPERIOR LABRAL ANTEROPOSTERIOR LESION

The labrum is a cartilaginous structure attached to the glenoid cavity which deepens the concavity surface and creates a more mechanically advantageous cavity for the humeral head. The labrum has a very similar design and serves a similar purpose to the knee meniscus. Superior labral anteroposterior (SLAP) lesion results from extreme external rotation of humerus while the shoulder is at 90° abduction, so one of the common injury mechanisms is throwing activity. While the arm is in the described shoulder 90° abduction position, a compelling traction force works together with the biceps power to generate a significant shearing force on the labrum which could cause the tear (Modarresi, 2011). Other contributing factors include overuse and direct trauma. Clinically, SLAP does not present on its own, and other shoulder pathologies will be seen as well (Burkhart and Morgan, 1990; Kibler, 1995; Meister, 2000).

## EVIDENCE ON ACUPUNCTURE FOR SHOULDER PROBLEMS

The majority of acupuncture trials have suffered from poor quality in design and insufficient information about the intervention (Green et al., 2005; Romoli et al., 2000). When assessing the quality of acupuncture studies, there are several critical factors that need to be addressed, apart from quality assessment criteria such as those published by the Cochrane Library or PEDro database (Moseley et al., 2002; van Tulder et al., 2003). The use of acupuncture points and the rationale of the selection must be defined clearly. For most trials, Traditional Chinese Medicine (TCM) approach was mentioned and a pool of acupuncture points was listed, but the number of needles used and the points selected for each individual subject were not reported. Secondly, in most trials, pain management is the primary outcome, but there should be consideration of the effect of acupuncture on a person's functional recovery and the use of the outcome measures other than pain, i.e. range of motion and functional outcomes need to be included. The third factor that needs to be considered is the definition of short term relief, long term relief and immediate postintervention pain relief. Lastly, the method of placebo or sham should be examined more closely.

One of the first studies of acupuncture for chronic shoulder pain was published in an English journal in 1976 by Moore (Moore and Berk, 1976). The study consisted of 42 patients, and the authors concluded that there was no significant improvement in shoulder discomfort between the treatment group and the sham. When acupuncture was compared with steroid injection, non-steroidal anti-inflammatory drug (NSAID), physiotherapy in the form of ultrasound, or placebo NSAID and placebo ultrasound, all interventions showed statistically significant improvement in shoulder pain and function at 4 weeks (Berry et al., 1980). Lin et al. (1994) compared electroacupuncture, regional nerve block and a combination of the two methods and demonstrated significant improvement in the group with combined treatment in pain control and mobility (Lin et al., 1994). Kleinhenz et al. (1999) treated 52 sportsmen with rotator cuff tendinitis in a single blind

randomised controlled trial (RCT) using non-penetrating sham needles as the control. Patients had eight treatment sessions over the course of 4 weeks. Acupuncture was more effective than placebo acupuncture in the treatment of pain. Constant-Murley score improvement was found to be significantly greater in the treatment group. Kleinhenz concluded that needling had integral therapeutic effects in treating athletes with chronic shoulder pain (Kleinhenz et al., 1999). Romoli et al. (2000) conducted an RCT involving 60 patients with unilateral shoulder pain. The patients were randomised into three groups: traditional acupuncture combined with mobilisation, ear acupuncture combined with mobilisation and mobilisation alone. This small pilot study showed some benefit of both traditional and ear acupuncture plus mobilisation over mobilisation alone.

In 2005, Green et al. published a systematic review on acupuncture for shoulder pain. Nine trials met the inclusion criteria, studying various shoulder disorders including adhesive capsulitis, rotator cuff disease and osteoarthritis (OA). When the quality of methodology was examined, the interventions of all trials were poorly described. Two trials assessed short term effects of acupuncture for a rotator cuff problem. There was no significant difference in short term improvement associated with acupuncture when compared to the sham. However, acupuncture was more beneficial than the sham in improving the Constant-Murley Score at 4 weeks. Green concluded that there is insufficient evidence to support or refute the use of acupuncture for shoulder pain in general. Nonetheless, there may be short term benefits with respect to pain and function (Green et al., 2005).

Since then, more trials have been reported. Two of these studies are of high quality and will be discussed in greater detail. Vas et al. (2008) recruited 425 patients in a multi-centre controlled randomised study, comparing single-point (ST38) acupuncture and placebo TENS as adjuncts to physiotherapy, analgesics and NSAID. The author concluded that acupuncture had better results in both shoulder function and pain relief than sham TENS (Vas et al., 2008). Molsberger et al. (2010) reported another trial for chronic shoulder pain with 424 subjects with shoulder pain for more than 6 weeks, known as German randomised acupuncture trial for chronic shoulder pain (GRASP). Subjects were randomly assigned to receive TCM approach acupuncture, sham acupuncture or conventional conservative orthopaedic treatment. The authors concluded that TCM acupuncture is an effective alternative to conventional orthopaedic therapy for pain at immediate posttreatment and at 3 months posttreatment.

## CLINICAL APPROACH

While the experience of using acupuncture in any chronic condition has been discussed in detail over the past 10 years, there is no general consensus on how to integrate acupuncture into a rehabilitation regimen for acute sport injury patients. However, it is the writer's opinion that active progressive shoulder exercises to restore the alignment and rebuild axial compression force are the most important treatment approach. Passive treatment modalities serve as adjunct therapies to support the recovery advancement of patients' conditions. Among all passive treatment modalities, experience shows that shoulder acupuncture consistently achieves good results.

As most of the clinical settings for sports medicine are managed by a multidisciplinary team including physical therapists, athletic therapists, chiropractors, trainers and physicians using conventional therapies described in the table, very often, acupuncture is only applied as an adjunctive treatment when improvement is guarded within a set time frame (Vas et al., 2008). However, as we have accumulated more evidence and clinical experience in acupuncture, incorporation of acupuncture could be done in a more integrated fashion and it could be applied at the acute phase.

In the acute phase, as a general rule, we should consider selecting distal acupuncture points only, compared to the sub-acute and chronic phases when we can select local points (Table 36.1). As mentioned, shoulder rehabilitation is very dependent on glenohumeral joint alignment and rotator cuff muscle axial compression force. To correct problems originating in alignment, in

TABLE 36.1 ■ Acupuncture point selection approach

Shoulder injury	Local acupuncture points
Bicipital tendonitis pain	LU2, LU3, LI14
Subscapularis tendonitis pain	LI15, LU2
Supraspinatus tendonitis pain	SI12, SI13, TE14
Infraspinatus tendonitis	SI11

addition to stretching and active postural muscle exercises, one could consider applying acupuncture to the related musculature. A recent case report by [Osborne & Gatt \(2010\)](#) described the effectiveness of acupuncture in scapulohumeral muscle myofascial trigger points among four elite volley ball players and the subjects experienced short term pain relief and improved function in the competitive phase. In our experience, acupuncture can alleviate the myofascial trigger point and connective tissue pain. As muscle and soft tissue are relaxed further, the patient can achieve a better result from the effect of stretching and soft tissue work. Also, the use of Shu points that are designated for cartilage and tendons should be considered as well. The points used in RCTs are summarised in [Table 36.2](#).

For tendinopathy, we can apply acupuncture with conventional therapies for inflammation and pain management. There is enough evidence from basic science to support the use of needles for both pain and inflammation. As pain and swelling reduce, the inhibition of muscle power from pain is less of a problem. Improvement in pain during rotator cuff muscle exercises will improve axial compression of the humerus on the glenoid cavity.

In our clinical experience, we use acupuncture in conjunction with conventional therapies in all phases of shoulder rehabilitation. The most important consideration is the selection of

TABLE 36.2 ■ List of acupuncture points used in RCTs of acupuncture shoulder conditions

	Kleinhenz et al. (1999)	Molsberger et al. (2010)	Dyson-Hudson (2007)	Vas et al. (2008)
TE14	X	X	X	
TE15	X			
SI9	X	X		
SI11	X		X	
SI12	X			
SI13	X	X		
SI14	X	X		
LI14	X	X	X	
LI15	X	X	X	
LU2	X	X		
LU3	X			
<i>Distal points</i>				
LI11	X	X	X	
SI3	X	X		
SI6	X			
GB34	X	X		X
ST38	X	X		X
TE5	X	X		

acupuncture points based on what phase the patient is in, and the cause of shoulder pain, i.e. alignment versus axial compression force, and the evidence we have collected from the all related published literature.

## COMMENTS

The current trend in clinical management of musculoskeletal injuries, the multi-modal approach, applies to shoulder problems. While there is no one single method that can address all clinical questions and challenges, the practitioner needs to be open to consider all available clinical evidence and integrate different interventions into the treatment regimen. As there is a moderate level of evidence for acupuncture in reducing pain and improving function, integrating acupuncture into patient treatment plans will be likely to benefit patients.

In general, as the patient feels less pain and stiffness and a decrease of myofascial tenderness, the treatment and exercises to correct glenohumeral alignment, improve muscle stabilisers, maintain the concavity compression and promote active range of motion and muscle power in the shoulder will become easier. Repeated use of acupuncture can improve the inflammation and swelling. Acupuncture can also be utilised in both the acute and chronic phase. However, the approach must be individualised, and the point selection will not necessarily be the same for all patients.

## Knee injury and knee pain

Surveys have shown that knee disorders constitute approximately 40% of sports injuries ([Majewski et al., 2006](#)). The anatomy of the knee sets the stage for likelihood of injury. The joint is located between two long levers (tibia and femur), and it relies on soft tissue structures for its strength and stability ([Magee, 1987](#)). The cause of knee disorders can vary, from overuse to trauma. Overuse knee injuries commonly occur due to repetitive knee bending and straightening, for example in running, cycling, rowing and volleyball. Knee injuries that result from trauma usually involve valgus or varus forces, twisting or deceleration movements, which occur in basketball, football, soccer and skiing ([Calmbach and Hutchens, 2003](#)).

In this section, common knee disorders will be discussed as well as their treatments and the common acupuncture protocols used to address them.

## PATELLOFEMORAL SYNDROME

Patellofemoral syndrome (PFS) is the most frequent single diagnosis among runners in sports medicine centres ([Dixit et al., 2007](#)) and is described as anterior knee pain involving the patella and retinaculum. Typical symptoms are stiffness or aching pain beneath or around the patella and a grinding/grating sensation with knee flexion. Pain can be aggravated by repetitive jumping (basketball, volleyball) and repetitive squatting (hockey goaltenders, baseball back-catchers) ([Dixit et al., 2007](#)). Biomechanical predisposing factors are over-pronation of the foot, asymmetrical quadriceps strength, and an increased 'Q' angle ([Dixit et al., 2007](#)). The 'Q' angle is the angle formed by a line drawn from the ASIS to the centre of the patella and a second line drawn from the central patella to the tibial tubercle. Normally the 'Q' angle for males is approximately 17° and for females approximately 14°.

Examination of the knee reveals a full range of motion, but flexion may produce grinding/grating as discussed earlier. Orthopaedic tests that are often positive are patellar mobility test, patellar apprehension test and patellar grind test. Palpation of the medial and lateral retinaculum may cause tenderness ([Dixit et al., 2007](#)). Radiographic imaging, CT scan and MRI are not usually required to determine a diagnosis.

## CHONDROMALACIA PATELLAE

Many practitioners believe chondromalacia patellae (CP) is the result of long-standing PFS and a diagnosis of CP should only be made when there is actual damage to the cartilage located on the undersurface of the patella. CP is commonly found in adolescents and young adults, and predisposing activities include running (soccer), jumping (basketball, volleyball) and twisting (snowboarding, skateboarding) (Yochum and Maola, 2009). The mechanism of this injury is frequently poor alignment of the patella gliding over the femur, which causes softening and fissuring of the cartilage located beneath the patella. Causes of CP may include trauma, patella dislocation, PFS and primary cartilage vulnerability (Yochum and Maola, 2009).

Patients suffering with CP may present with similar symptoms as PFS. Examination often reveals genu valgum, patella alta, quadriceps atrophy, increased 'Q' angle and positive Clark's sign. Radiographs may assist in diagnosis if a skyline view is requested, but an MRI will provide the most diagnostic information (Yochum and Maola, 2009).

## KNEE OA

Generally, knee OA affects 10% of the general population over 55 years of age (Peat et al., 2001). Many studies in recent years have concluded that previous sports-related knee injuries predispose individuals to future knee OA. For example, anterior cruciate ligament (ACL) injuries sustained during sports have been found to cause an increase risk of future knee OA (Lohmander et al., 2004). Another study found that 10–20 years following a diagnosis of a ACL or meniscus tear, 50% of the subjects suffered with knee OA symptoms of pain and decreased function (Lohmander et al., 2007). Athletic patients with knee pain due to OA are common referrals to our sports medicine clinic. Other risk factors that predispose an individual to knee OA are: increased body mass index (BMI) and family history (Zhang et al., 2010). Signs and symptoms associated with knee OA often include mild joint swelling, bony enlargement, atrophy of muscles surrounding the knee, crepitus/grinding over the range of motion, morning stiffness lasting less than 30 min, and aggravation of pain with activity (Felson, 2006).

Positive examination findings for knee OA are restricted active/passive ranges of motion and tenderness of bony enlargements. Radiographs will help confirm diagnosis in addition to a detailed history and examination (Lohmander et al., 2004).

## ANTERIOR CRUCIATE LIGAMENT TEAR

ACL tears are found in both contact and non-contact sports. Non-contact injuries account for 70% of ACL tears, which occur during deceleration of the lower extremity, with the quadriceps contracted and the knee at or near full extension (Shimokochi and Shultz, 2008). A few examples in the common non-contact sports are skiers and snowboarders falling backwards and soccer players performing sudden cutting (when athlete changes direction abruptly) movements. Patients often feel immediate pain and hear a 'pop' at the time of injury followed by immediate swelling. A comment often made following an ACL tear is a feeling of the 'joint giving way' or the patient might display the 'double fist' sign, by placing their fists together and rotating them in a grinding motion (Cimino et al., 2010).

Examination of a possible ACL injury may be difficult initially due to joint haemarthrosis and patient guarding. Knee range of motion will be restricted predominately in flexion. The three most accurate orthopaedic tests to perform are: Lachman Test (sensitivity 85%, specificity 94%), Knee Anterior Drawer Test (sensitivity 92%, specificity 91%) and Pivot Shift Test (sensitivity 24%, specificity 98%) (Benjamise et al., 2006). Radiographs are helpful to rule out an avulsion fracture, but MRI is the preferred imaging for diagnosing an ACL tear (Cimino et al., 2010).

## MENISCAL TEARS

It has been reported that 33% of meniscal tears are associated with sports activities (Manson and Cosgarea, 2004). The mechanism of a meniscal tear is often rotation on a fixed tibia with either knee flexion or extension. High risk sports involve quick twisting movements of the knee such as soccer, baseball, tennis and basketball. The patient may complain of gradual onset of effusion, pain when walking up or down stairs, pain with squatting or kneeling and locking of the knee (Johnson, 2000). An interesting note should be mentioned that 60–75% of patients with ACL tears also present with meniscal tears (Cimino et al., 2010).

Examination of the knee may find restricted range of motion, localised joint line tenderness (sensitivity 75%, specificity 77%), positive McMurray's Test (sensitivity 55%, specificity 77%) and positive Apley's Compression Test (sensitivity 22%, specificity 88%) (Meserve et al., 2008). Diagnosis using MRI can also provide pertinent therapeutic information (McNally, 2002).

## COMMON KNEE TREATMENTS

Since the mechanisms of injury for PFS, CP and OA are similar, it is understandable that their treatment options are similar as well. Therapy goals are to correct the biomechanics of the knee, hence, a few of the common therapy choices are: strengthening the quadriceps and/or vastus medialis (Fransen et al., 2008; Jensen et al., 1999; Whittingham et al., 2004); correcting foot mechanics by incorporating shoe orthotics; stretching surrounding hypertonic musculature (i.e. iliotibial band (ITB), hamstrings, gastrocnemius, soleus); and using electrical modalities (i.e. TENS, ultrasound, interferential current (ITC), laser) (Rutjes et al., 2009; Silva et al., 2008).

On the other hand, ACL and meniscus tears are more traumatic requiring proper diagnosis and a critical decision whether surgery is required. Nevertheless, these types of tears still require a strengthening programme to prevent further injury or to aid in postoperative rehabilitation (Ericsson et al., 2006; Risberg and Holm, 2009).

## EVIDENCE ON ACUPUNCTURE FOR KNEE PAIN

In recent years acupuncture has become a mainstream form of treatment. It is quite exciting for health-care practitioners because this provides another option to help treat patients. In an analysis of United States national data in which 2 million acupuncture users were surveyed, 44% of the individuals sought acupuncture because conventional treatments did not help, 57% felt combining acupuncture with conventional medical care would be beneficial and 25–35% of the respondents indicated that conventional medical professionals recommended acupuncture (Burke et al., 2006).

There have been several promising studies into the acupuncture treatment of knee OA and PFS, which have concluded that acupuncture decreased pain and improved functioning (Jensen et al., 1999; Kwon et al., 2006; Naslund et al., 2002. See also Chapters 19 and 35). Also, there has been evidence to support that these improvements are long term (White et al., 2007). In a large RCT, Berman et al. (2004) studied the effect acupuncture had on knee OA. Once again, the acupuncture group experienced significant reduction in pain and improved functioning. In another systematic review examining knee OA, which was also supported by a Cochrane Review, the authors concluded that acupuncture again proved to be more effective for pain reduction and improvement of function than sham acupuncture and no additional treatment (usual care) for patients with knee OA. The authors also added that acupuncture should be considered as an alternative to treatment with NSAIDs (DARE, 2012; White et al., 2006). In a recent systematic review by Manheimer et al. (2010), 16 RCTs were evaluated which studied true acupuncture's effect on OA of the knee, hip and hand. Once again, the authors concluded that true acupuncture, when compared to waiting list and another active care control groups, did improve the patient's OA pain and functioning (Manheimer et al., 2010). In other research,

acupuncture has been found to be safe and cost-effective (Melchart et al., 2004; Reinhold et al., 2008; Whitehurst et al., 2011). Researchers found serious side effects to be rare; most frequent adverse reactions were needling pain and hematoma.

Clinical points

High quality evidence confirms the effectiveness and cost-effectiveness of acupuncture for treating knee OA. Acupuncture is recommended in guidelines.

As more diverse health-care practitioners use acupuncture in their various disciplines, acupuncture’s role as an adjunct to different types of treatment is being witnessed (Mao and Kapur, 2010). In a study by Witt et al. (2006), researchers concluded that acupuncture plus routine care showed marked improvement in patients with chronic OA associated pain of the knee or hip. This conclusion is also supported by another study that found acupuncture is being utilised with increased frequency as an adjunct or alternative to both pharmacologic and non-pharmacologic treatment of knee OA and is a common reason for referral for acupuncture (Burke et al., 2006). It has been stated that since there is no definitive cure for knee OA, the goal of many treatments, including acupuncture, is to decrease pain and improve function in order to delay knee replacement surgery (Mao and Kapur, 2010).

CLINICAL APPROACH

There is little or no consensus in sports rehabilitation on how to integrate acupuncture into a treatment regimen for acute sport injury patients. However, it is the writers’ opinion that proprioceptive, muscle balancing and close kinetic chain exercises to establish the patella alignment and restore proper muscle balance are essential elements in the treatment approach. Passive treatment modalities such as acupuncture serve as important adjunct therapies to improve the outcomes of the patients’ conditions. Among all passive treatment modalities, experience shows that knee acupuncture consistently attains excellent outcomes.

Acupuncture treatment has been found repeatedly to both decrease pain and improve functioning, benefitting patient management by several different health-care professions. In our clinical experience, pain reduction produced by acupuncture allows for the quicker initiation of a strengthening programme, indirectly aids in improving joint mobility and range of motion and also has a positive effect on hypertonic tissues.

In our clinical experience, we use acupuncture in conjunction with conventional therapies in all phases of knee rehabilitation. The most important consideration is the selection of acupuncture points based on what phase the patient is in and the cause of knee pain, i.e. meniscal, ligamentous or bony causes.

Table 36.3 summarises the knee disorders that have been reviewed and examples of local points to use (Trinh, 2012).

TABLE 36.3 ■ Acupuncture points used for various knee conditions

Knee condition	Acupuncture points
Patellofemoral syndrome	ST35, SP9 (SP10)
Chondromalacia patellae	ST35, SP9 (SP10)
Knee osteoarthritis	ST35, <i>Xiyan</i> (XL2), SP9, UB40
Anterior cruciate ligament	<i>Xiyan</i> (XL2), ST35, SP9 (SP10)
Meniscal tear	<i>Xiyan</i> (XL2), SP9, ST35

## CONCLUDING COMMENTS

Knee injuries are commonly seen in a sports medicine clinic setting. Research has found acupuncture can play a supporting role in the treatment of these injuries not only to relieve pain but also to improve functioning. New research is looking into acupuncture's efficacy in treating different conditions, as well as its role as an adjunct therapy. Nonetheless, health-care practitioners have another safe and promising treatment to offer to their patients.

Knee and shoulder conditions are commonly seen in sports medicine clinic. Acupuncture is a useful technique to incorporate along with other rehabilitation techniques. Successful treatments of these conditions will play an important role in enhancing athletic performance.

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# Acupuncture in primary care

J. Foell

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## **What are the characteristics of primary care?**

Primary care, also known as family practice or general practice, is the care environment which can be accessed without prior referral. It is the entry point into the healthcare system, not regulated by disease labels. The World Organisation of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) describes generalists in primary care as ‘specialist physicians trained in the principles of the discipline. They are personal doctors, primarily responsible for the provision of comprehensive and continuing care to every individual seeking medical care irrespective of age, sex and illness. They care for individuals in the context of their family, their community, and their culture, always respecting the autonomy of their patients. They recognise they will also have a professional responsibility to their community. In negotiating management plans with their patients they integrate physical, psychological, social, cultural and existential factors, utilising the knowledge and trust engendered by repeated contacts. General practitioners/family physicians exercise their professional role by promoting health, preventing disease, providing cure, care or palliation and promoting patient empowerment

and self-management. This is done either directly or through the services of others according to health needs and the resources available within the community they serve, assisting patients where necessary in accessing these services' (Allen et al., 2011). In people-centred primary care the relationship is theoretically unending – from womb to tomb, from the cradle to the grave.

Family practitioners work in 'ultra-long, ultra-brief' relationships with their patient (Launer, 2002). Family practice is situated in a field of tensions. Colluding with the individual patient might mean colliding with the requirements of rationing for the sake of the public at large. Treatment of the individual care-seeking person might not be in line with disease-specific guidelines for the specific population. Gatekeeping is the term for the pastoral activity of managing tight healthcare resources for a given population. It requires high healthcare-system literacy, judgement about the appropriateness of the different care environments and medical cultures in a given situation, and careful negotiation skills. Some authors see this conflict of interest epitomised in the role of the double agent (Weingarten et al., 2010).

## RESPONSIBILITIES

The role of the primary care physician includes several responsibilities. The interests of the individual, the population, the provider organisation and societal values need to be balanced – just as managing a surgery list means being simultaneously immersed in the story of the immediate clinical encounter and being aware of the situation in the waiting room and other areas of the care environment. Therapeutic work in relationships includes containing and holding (Cocksedge et al., 2011; Ridd et al., 2012). Primary care consultations are densely packed multi-topic conversations including patient-generated and service-generated activities, reactive and proactive care. Structured care programmes for long-term conditions form an increasing part of the care. The quality of managed care (which often affects payment) is measured by the electronic recording of care activities. Information technology has changed the character of primary care. The computer plays an increasingly important role as active participant in the consultation, as physical object in the room and as embodied authority (Silverman and Kinnersley, 2010). The voices of all the stakeholders in the therapeutic relationship are encapsulated in the electronic patient record. Prompts direct the attention of the clinician to the patient as part of a group, and generate an attention dilemma (Swinglehurst et al., 2011). It takes time to engage with the body and the story of the patient. In the context of acupuncture in primary care, the recorded information matters. The way in which presenting complaints, negotiation with the patient and the management is recorded, may either legitimise, or impede access to, interventions (e.g. acupuncture officially endorsed for low back pain, but not for OA of the knee) (Table 37.1).

## FUNDING

Third-party funding for primary care services differs across healthcare-systems. Services may be funded by the taxpayer, by insurance companies with dual contributions from employers and subscribers, and also by managed care organisations (Duran et al., 2005). Reimbursement for services in primary care may include capitation fees, fees for services and lump sums for quality measures of disease-management. The range of services which are included in a contract varies widely between systems. It depends on specific policies whether acupuncture can be delivered via third-party funding. Personal add-on contributions for individual services exist in Germany. Some primary care based acupuncture services in the UK use voluntary donations from patients to account for the price of needles and practitioners time.

## ACCESS

Depending on the specifics of the healthcare system, access may be regulated by area or may allow patients to make their own choices.

**TABLE 37.1 ■ Diagram showing care paradigms (WHO Report on Primary Care) (van Lerberghe and Evans, 2008)**

<b>Conventional ambulatory care in clinics or outpatient departments</b>	<b>Disease control programmes</b>	<b>People-centred primary care</b>
Focus on illness and cure Episodic curative care	Focus on priority diseases Relationship limited to programme implementation	Focus on health needs Comprehensive, continuous and person-centred care
Responsibility limited to effective and safe advice to the patient at the moment of consultation	Responsibility for disease control targets among the target population	Responsibility for the health of all in the community along the life cycle, responsibility for tackling determinants of ill health
Users are consumers of the care they purchase	Population groups are targets of disease control interventions	People are partners in managing their own health and that of their community

## Who delivers acupuncture in primary care?

### PROFESSIONS, WORK CULTURE, OTHER CO-INTERVENTIONS

Patients may be treated with acupuncture by various professionals with varying theoretical underpinning and varying professional governance structures regulating their practices. It may be a doctor with added training in acupuncture. It may be a nurse, midwife or other healthcare worker who specialises in acupuncture. It may be a physiotherapist or a podiatrist. It may be an acupuncturist trained only in acupuncture who is voluntarily regulated by his professional organisation.

### ACCESS CRITERIA

Access to services without prior referral is the hallmark of primary care. Fluidity and generosity, the ability to respond adequately to the dimensions of a condition, are key elements of primary care. Access to acupuncture within the realm of primary care may have hard and soft obstacles – as soon as an internal referral is needed, issues of governance, capacity management and access criteria assume importance. Some degrees of flexibility may be lost in the process. Some services may be condition-specific (OA knee, chronic pain, menopause clinic, addiction clinic), and their availability is part of the normal variation in care provision. In the UK there are official (Care closer to home) and unofficial (referral management schemes) incentives to reduce clinical activities in secondary care (Department of Health, 2011). As part of the redistribution of services into primary care, opportunities to provide acupuncture have arisen, often in musculoskeletal domains or under the banner of chronic pain (Harvey and Orpen, 2010).

## The context of acupuncture in primary care

### BRIEF ACUPUNCTURE INTERVENTION VS. DEDICATED SERVICE

Acupuncture may be delivered as a brief intervention within the routine consultation as a response to an acute problem (pain or nonpain-condition) or even to change the character of a relationship and enrich it by the dimension of bringing in a direct healing element. It starts a different dialogue, mediated by caring and touch (Adler, 2002; Sambo et al., 2010). Very little is known about the effectiveness of these interventions. It has not been possible yet to ascertain exactly who offers these interventions to whom and under what circumstances. Observations

from peer support groups and medical acupuncturists, who practise these interventions as part of their routine practice, suggest that ‘miracle cures’ (i.e. dramatic immediate symptomatic relief) are most likely to be encountered in this setting, and these broaden the horizon of the acupuncturist (Freedman, 2012). The downside of brief interventions is that feedback is difficult to get. Patients may be left undertreated in terms of a ‘course’ of somatosensory stimulation. It is fascinating to observe the responses of people who didn’t expect therapeutic needling to be offered and responded to a novel intervention. This is in contrast to services aimed at chronic conditions such as widespread body pain, or generalised pain disorders, the treatments of which necessitate a higher therapist input in terms of the number of sessions, duration, type and degree of needle stimulation and needle count, and therefore has implications for service capacity (White et al., 2008). Long waiting times for acupuncture for chronic conditions are commonly encountered. To run a dedicated acupuncture service requires a minimum of logistics – space, administrative support and a network in the practice environment which facilitates this approach. The ability to respond flexibly to circumstances, to tailor treatment to the needs of patients and to improvise within given constraints is one of the key strengths of generalists. Acupuncture as an add-on treatment can enrich this kind of care.

What drives doctors to take on the role of therapists, using touch and personal contact as a treatment modality? (Dunbar, 2010; Singh and Leder, 2012; Gallace and Spence, 2010) Again, little is known about the motivation of doctors engaging in hands-on therapies. Frequent comments encountered during learning-needs-assessments in training courses are that there is an unmet need in the population. Clinicians report a gap between what can be done with usual care (giving medication) and the need to pass cases on, knowing that the compartmentalised care-system does not allow holistic treatments in services which are accessed by referrals to specialists. These clinicians assert a desire to offer more to patients and also to reduce referral rates.

## COMMISSIONED SERVICES IN PRIMARY CARE

The terms and conditions, rules and regulations for services offering acupuncture vary widely. They may be available solely for the people registered with the practice, managed by the practice or offered by the local Health Trust or for collaborating clusters of practices. These ownership and funding arrangements have consequences for onward referral processes, and more importantly, for secondary work such as audit or outcome measurements. The latter is of the highest importance: service purchasers increasingly want to see outcomes – but administrative work (getting people to fill out sophisticated questionnaires, populating databases, producing statistics) is often more challenging than simply delivering a service. The implications for workload and administrative support can be significant.

## ACUPUNCTURE AS COMPLEX INTERVENTION

What else besides purposeful needlestick injuries is in the black box? Undoubtedly acupuncture is a multimodal intervention (Lundeberg and Kurosawa, 2010). The needling component itself has effects on various physiological pathways. The perceived quality of the interaction, the practitioner effect and effects relating to the therapeutic relationship, and social learning, add other dimensions to this complex intervention (Kelley et al., 2009; White et al., 2012; Kaptchuk, 2002; Colloca and Benedetti, 2009; Kirmayer, 2004; Conboy et al., 2010). Depending on the set-up of the service, environmental factors like the location in which the service is delivered, the personalities of the therapists and the working culture of the provider organisation are components of the intervention. Very little is known about the status of these factors in the complex intervention. Are they mediators, predictors or moderators? (Berk et al., 1977; Kraemer et al., 2001).

## IDEOLOGICAL ISSUES

Therapeutic needling can happen in very different conceptual frameworks – in the time-pressured environment of a GP consultation, alongside musculoskeletal assessments and exercise-based interventions in a physiotherapy clinic, delivered by nurses in a chronic pain clinic, at home or in a hospice in a palliative setting or in one-to-one situations or a group setting by subcontracted acupuncturists (Dale, 1996; Hopton et al., 2012; Unwin and Peters, 2009). Interactions – what is talked about, how it is talked about – are also shaped by organisational practices and underlying worldviews (Bishop et al., 2012; Paterson and Britten, 2008). Patient-provider interactions in the independent sector have attracted considerable research, mainly in qualitative studies (Gale, 2011; MacPherson et al., 2003; Hartog, 2009). Patient-centred consulting is an essential topic of medical education. There is a rich research and education tradition exploring this concept (Ong et al., 1995; Henbest and Stewart, 1989; Stewart et al., 2000; Baarts et al., 2000; Matthias and Bair, 2010; Mead and Bower, 2000). Very little is known about its relation to hands-on therapies, which may be delivered within this context. It is theorised that the clinical inquiry underpinned by the conventions of traditional Chinese medicine (TCM) explores more interactions of diet, lifestyle and pain experience, in contrast to the more body-region focused investigation based on the Western medical tradition (Paterson and Britten, 2008; Paterson et al., 2012; Rugg et al., 2011).

## FUNDING

Acupuncture services relate to various clinical domains – pain, maternity, end of life, sports and exercises, mental health and addiction, women's health. They may encompass the whole range, delivered by practitioners who feel clinically competent and confident to fit the therapeutic intervention into the clinical landscape. This requires confidence and psychological flexibility. Often acupuncture is delivered as an add-on intervention alongside other treatments within the condition-specific setting. Acupuncture is rarely delivered within third-party-funded services as an independent modality clinic. It is usually part of something else. Therefore funding for acupuncture services is not considered a priority: it is an add-on. Acupuncture sits between medical procedure and social care giving and has to fight for funding opportunities. This has implications for service development and governance. It depends on active enthusiasts and trusted relationships, but it is not part of institutional traditions.

## Person, people, populations

### ALWAYS TROUBLE WITH THE CATEGORIES

Musculoskeletal conditions are repeatedly reported as forming a large proportion of the workload in primary care (Hasselström et al., 2002). Epidemiological studies are based on surveys and analyses of consultation codes in primary care databases (Macfarlane et al., 2001). Chronic pain is not represented by one generally agreed definition (Nordin et al., 2006; Khan et al., 2010; Jordan and Croft, 2008). In contrast to other long-term conditions like diabetes or hypertension, information about musculoskeletal conditions is scattered amongst the database's categories. Musculoskeletal pain is commonly coded by affected body region. Musculoskeletal conditions rarely present in isolation, and rarely in one body region only (Carnes et al., 2007). They also commonly have central features like fatigue and sleep disturbance (Apkarian et al., 2009). Longitudinal studies document how musculoskeletal complaints in the axial skeleton and the limbs accumulate over time (Kamaleri et al., 2009; Rohrbeck et al., 2007). Instead of a picture of a sequence of separate episodes a quite different picture emerges: 'The question is not "have you got it"? But "how much of it have you got"?' (Croft, 2009). The consequence of this concept is the recognition of the central features many musculoskeletal conditions share (Yunus, 2008; Meeus and Nijs, 2007).

Establishing the degree of peripheral and central contributions to the pain experience, as ‘emergent phenomena’ of the brain, is as difficult as it is important (Gwilym et al., 2010, 2011; Ge et al., 2009; Affaitati et al., 2011; Smart et al., 2010). At one end of the spectrum are ‘brains in jars’, treated with psychotropic agents. At the other end are postural imbalances, degenerative changes and changes in somatic tissue texture, treated with endless courses of interventions (Clauw, 2009; Dadabhoy et al., 2008; Epstein et al., 1999). One explanatory model for chronic pain favours a centripetal direction, the ‘endorgan-dysfunction-model’. The centrifugal model proposes ‘altered nervous system processing’ (Apkarian et al., 2011). Behavioural changes are the norm (Crombez et al., 1999). ‘Fibromyalgia’ or ‘somatoform pain disorder’ may be the diagnostic label for such a situation, but coding practices vary widely. Applying a diagnostic code for a condition with ambiguous meaning has ethical consequences. The usefulness of such a label without consequences for therapeutic action, or without increased understanding of their situation for individuals, is controversial (Hughes et al., 2006; Sim and Madden, 2008; Undeland and Malterud, 2007). Chronic widespread pain and fibromyalgia are not just medical conditions affecting individuals. They affect relationships, and living with these limitations is a team-game. They have a dominant social dimension (Schwartz et al., 1991; Turk et al., 1987). Diagnoses like ‘fibromyalgia’ or ‘somatoform pain disorder’ can be medical codes for social suffering.

## THE SOCIAL DIMENSION

The degree to which clinicians have to engage with social suffering varies widely (Carr-Hill et al., 1996). The scope of a practice in a leafy suburb differs significantly from one in a market town or in a deprived inner city district, a rural environment, remote area and differs again from a population-specific service like an outreach service for the homeless. The scope of practice and exposure to different social groups shape the perspective of the therapist. Chronic widespread pain can be part of stress-related disorders (de Kloet et al., 2005; McFarlane, 2007). The ability to cope with adversity has to do with the resources available to the sufferer and the burden an individual has to carry (McEwen, 2010). Factors like adverse childhood experiences or exposure to domestic violence/intimate partner violence shape the illness trajectory over a lifetime and also the lives of the children (Von Korff et al., 2009; Coker et al., 2005; Jones et al., 2009; McBeth et al., 1999; Bardes et al., 2001). Similar considerations apply to the conditions presented by migrants from war-torn countries (Bhui et al., 2003; Kirmayer, 2002, 2007; Cook and England, 2004; Hinton and Lewis-Fernández, 2010; Löfvander and Furhoff, 2002). The experience of being excluded intensifies the pain experience even in experimental conditions with healthy volunteers (Eisenberger et al., 2003). One can only imagine what it looks like in real life with repeated negative events over a lifespan, shaped by the transmitted experiences of close significant others who were socialised in similar conditions.

The intrusion of chronic widespread pain or, to be more precise, the ability to live the life one wants to live despite adversity, is like other conditions associated with socioeconomic status. Health inequalities matter. The scope of practice in socially deprived areas or for marginalised people asks for different activities and service specifications (Jordan et al., 2008; Fiscella and Epstein, 2008; Feldman, 2006). A group of GPs from deprived areas in Scotland recently formed an association under the banner of the ‘deep end’, an area of practice where social dimensions are placed in the foreground (Mercer et al., 2007; Watt et al., 2008; Watt, 2004, 2011, 2012). What value or significance would hands-on-nonspecific-effects-interventions have in these circumstances?

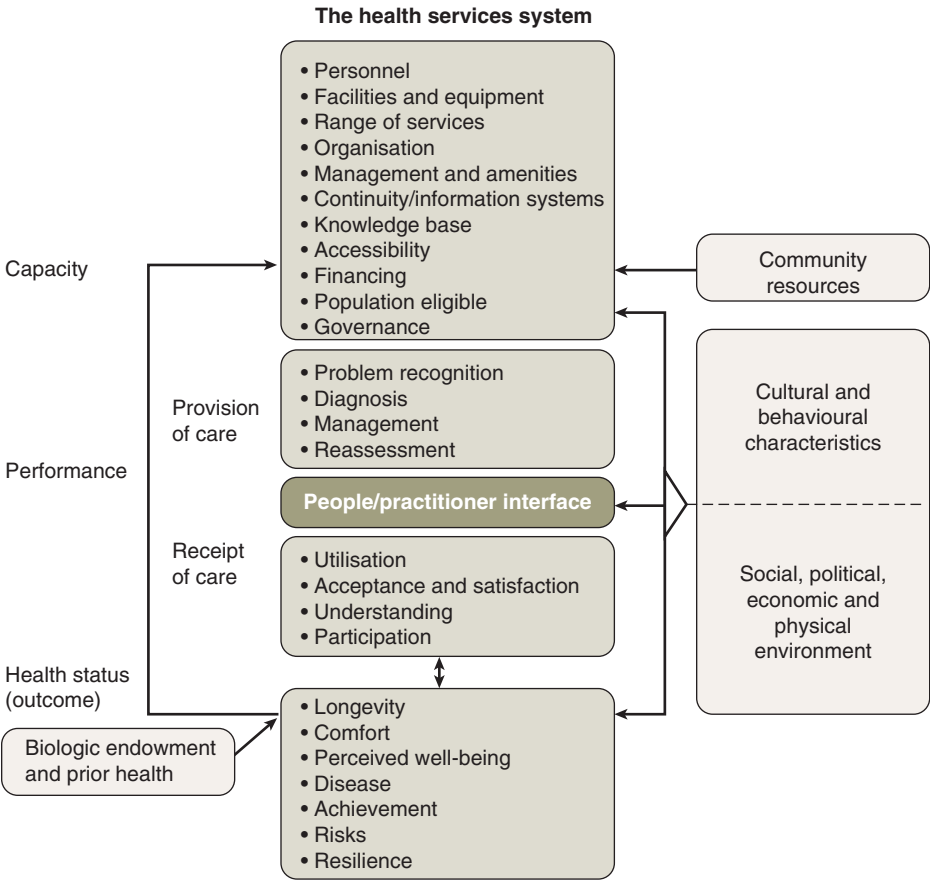
## ARE SOMATISERS FREQUENTLY ATTENDING WITH MEDICALLY UNEXPLAINED SYMPTOMS?

There are many ways to look at the group(s) of people who make most visits to their doctors. The Pareto principle applies: 20% of the practice population account for 80% of the workload (Pareto, 1964; Heywood et al., 1998). What characterises them? (Gili et al., 2011) Looking

from afar, some features seem to stand out: a combination of pre-existing diseases, anxiety, low health literacy, low socioeconomic status and dysfunctional attachment styles (Katon et al., 2001; Townsend, 2008; Scaife et al., 2000; Vedsted et al., 2001). But if the focus sharpens and one is looking from close-up, things are not so obvious any more (Vedsted and Christensen, 2005). Interventions that only address the patients themselves made little difference (Smits et al., 2009). Only a combined intervention with components directed both at the provider organisation, and at the individuals, showed some changes (Bellon et al., 2008). Each component of the categorisation given earlier has been criticised as misleading. Somatisation as a concept illuminates more the ideological stance of the medical system (Crombez et al., 2009; Kirmayer and Young, 1998; Sharpe and Carson, 2001). ‘Medically unexplained symptoms’ are the administrative term to classify the miscellaneous unclassifiable clutter, after the spectrum of presenting symptoms has been organised. It is unlikely that a charity for patients suffering from ‘MUS’ will ever be formed. The function-orientated Eastern approach seems to be a more appropriate concept for dealing with ‘medically unexplained symptoms’ (Tan et al., 2004). Indeed a randomised controlled trial (RCT) investigating the effect of TCM-based acupuncture added to usual care showed increased levels of wellbeing in the treatment group (Paterson et al., 2011). However, no change in the consultation patterns was demonstrated. Critical voices have suggested different wording for the acronym ‘MUS’ to create a conceptual space which allows patients and practitioners to have a different conversation: ‘Medically unexplored stories’ or ‘medically untreatable symptoms’ (Launer, 2009). It leads the way back to the basic questions: ‘What ails you?’ ‘Why are you here?’ (Soler and Okkes, 2012; Frank, 2005).

## THE COMORBIDITY CHALLENGE

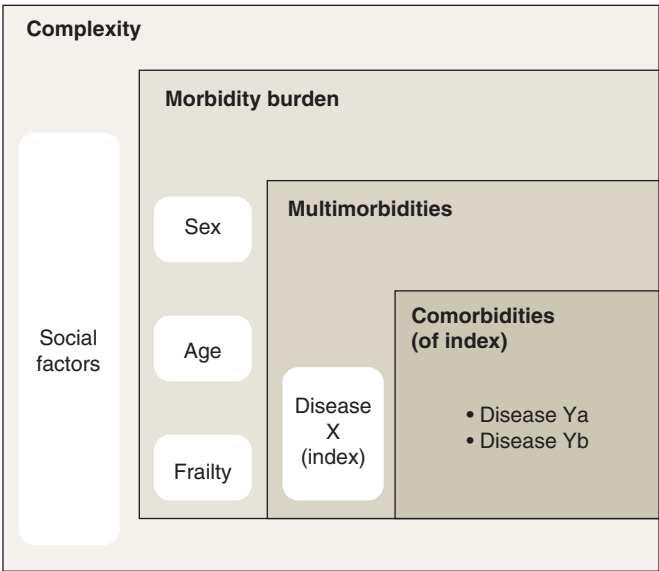
Comorbidity is the occurrence of one or more unrelated conditions in an individual with any given condition (Fig. 37.1). Multimorbidity is the co-occurrence of biologically unrelated illnesses (Valderas et al., 2009). Comorbidities – mental health problems – widespread body pain: Could it be that these categories serve only as different conceptual lenses? (Aggarwal et al., 2006; Mewes et al., 2009) Are they looking at the same patient group, only with different terms and ways of making sense? (Foell, 2013) Listening to patients’ storeys makes us quickly understand how upbringing and living conditions contribute to the currently experienced pain. It is often not pain alone that is the problem; presenting pain just brings existential suffering to medical attention (Biro, 2010). Chronic pain is often associated with other medical conditions (Bair et al., 2008; Mäntyselkä et al., 2008; Niles et al., 2005). Unfortunately these factors are often not included in the design of the studies which inform policymaking for musculoskeletal conditions (Boyd and Fortin, 2010). They are regarded as a contamination which had been excluded in the process of getting pure information from a study. Primary care is full of uncertain and ambiguous situations (Schön, 1991). Consultations have a ‘high noise-low-signal’-ratio, but for chronic pain and mood disorders, the noise itself is the signal. In this environment of high clinical uncertainty and high symptom pressure, information derived from RCTs may not be helpful in the treatment of patients with multiple comorbidities (Fortin et al., 2006). Peripheral and central pain mechanisms, enacted and embodied in an environment that directs a spin towards persistent pain intrusion as stress-related condition, can make categorising problems a very difficult task. The term ‘comorbidities’ can be broken down into several concepts (Valderas et al., 2009). Diseases do not exist a priori. They are not natural objects. They are man-made agreements, and like any epistemological concept, change over time (Rosenberg, 2002; Jutel, 2009). Recent years have also seen thresholds for treating diseases getting even lower and the norms for separating the normal from the abnormal, with implications for treating the deviance from normality, getting changed (Thorpe et al., 2005). The borderline between risk factors for a disease and the criteria to establish the diagnostic label of a disease has become blurred (Aronowitz, 2009; Bell and Figert, 2012).



**Figure 37.1** Diagram of the primary care landscape (Starfield, 1998).

It is not only the concepts that change, diseases with established and relatively stable definitions also change in the face of societal development – infections, for example, have undergone dramatic changes in recent history (Jones et al., 2012).

Similar phenotypes may have different aetiologies. This has consequences for the choice of therapeutic strategy (Fig. 37.2). Pleiotropy describes how one factor may cause diseases in different body systems – the presence of smoking for example can generate different diseases such as lung cancer, essential hypertension and periodontal disease. These factors may even interact and add towards the severity of the progression of the disease. Etiological heterogeneity describes how one disease is the result of the interaction of different, unrelated risk factors – ischaemic heart disease is one example. There are also episodic, relapsing remitting conditions such as chronic musculoskeletal pain, abdominal pain or headaches. They behave like chronic conditions but are not classified as chronic conditions. The same applies to depression. In most situations, apart from lung cancer, there is not a single cause for a single condition – the health problem a person is living with is the result of interacting factors over the span of a lifetime, from womb to tomb (Starfield et al., 2005; Valderas et al., 2009).



**Figure 37.2** Comorbidity constructs (after Valderas (2009) *Ann. Fam. Med.* 7, 357–363).

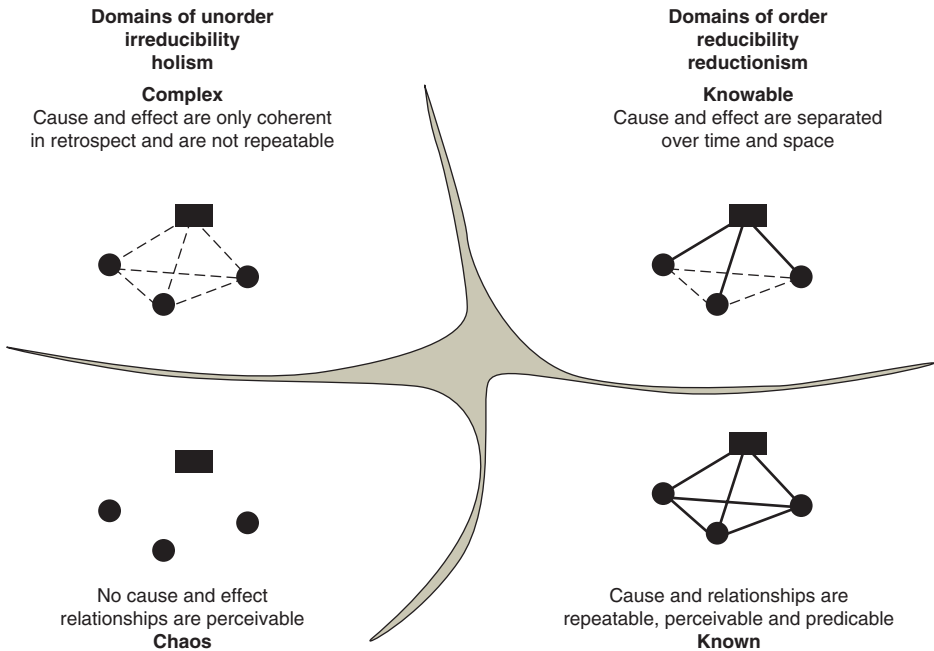
**ARE MEASURES OF COMPLEXITY THE ANSWER?**

And why do we have problems with these situations? How can we best help? Which tools are helpful? ‘Complexity’ stands for the unease the healthcare system feels about uncertainty (Katerndahl et al., 2010). In clinician-talk, ‘complex’ describes a situation where clinical algorithms are inadequate to manage the problem. It may trigger the call for a multidisciplinary team to act as authority. The task may be to *do* the job or to back up *not* doing the job. The presence of a coordinated multidisciplinary team indicates the assumption that the task is possible, but difficult. Interprofessional and multidisciplinary teamwork of highly specialised healthcare practitioners within an infrastructure which can accommodate these time- and labour-intensive tasks exists for this situation. Complexity describes the unpredictable interaction of factors and even the emergence of a phenomenon which cannot be attributed to a single cause.

The challenge of having to coordinate care for troubled individuals outside the regulated (dis-) comfort-zone of clinical algorithms leads to attempts to map the factors which cause the problem (Fig. 37.3). Five domains have been identified and graded in severity – illness factors, relationship factors like the readiness to engage, social factors like housing and support, health system factors like multiagency involvement and resource-factors like insurance cover and language (Peek et al., 2009). Although this framework can grade the complexity of a case, it is arguable how useful this is. If the desired outcome – having more resources and more time to coordinate the existing workforce – is not available, what is the consequence of the ability to map the size of the challenge?

**CONTEMPORARY FORMULATIONS FOR BODY-MIND-ENVIRONMENT INTERACTIONS**

How does ‘the social’ get under the skin? Life is unfair. Health inequalities exist. Social ranking plays a huge role in the severity and intrusiveness of illnesses. The likelihood of being exposed to physical and emotional trauma, and also the resilience to cope with this asymmetrically distributed



**Figure 37.3** Framework of sense-making, squares are causal agents, circles effect-agents (Sturmberg, J.P., Martin, C.M., 2009. Complexity and health - yesterday's traditions, tomorrow's future. *J. Eval. Clin. Pract.* 15(3), 543–548).

load, is linked to social position (McEwen, 1998; Davies et al., 2009). Chronic widespread pain neither exists in isolation from other comorbidities, nor is a predicament which has been randomly scattered over the population (Nicholl et al., 2009). The effects of having a vulnerable position in society affect every level of organisation, from the molecular to the molar level, to personhood and relationships (Kirkengen Al, 2007; Gianaros and Manuck, 2010). Increasing evidence mainly from the research field of biological psychiatry captures the effect of gene-environment interactions and vulnerable junctures in which a predisposition may lead to the manifestation of disease (Gregory et al., 2008; Koenen et al., 2008; Insel Tr, 2010; Braff et al., 2007). At least on a theoretical level, the dynamic interactions of nature and nurture became more transparent, and may inform how practitioners deal with those who come to seek help (Edwards et al., 2008). The previously rigid boundaries between structure and function became fluid. We see morphometric changes in brain areas corresponding with afflictions like depression and chronic pain (May, 2008). Sophisticated technologies have visualised altered molecular signalling and changes in brain circuits (Apkarian et al., 2009, 2011; Tracey and Mantyh, 2007). New knowledge about neural plasticity, immunology, epigenetics and epidemiological studies has dynamised Western medical research (Marmot et al., 1991; Holliday et al., 2010). However, transferring this general knowledge to individual patients and their particular predicaments is difficult. This new body of knowledge has very few consequences for the field of medical care for chronic pain and social suffering.

## WHAT DOES IT MEAN FOR CARE ORGANISATION? HOW CAN THE BURDEN OF COMORBIDITIES BE MEASURED?

As discussed earlier, we deconstructed the concept of diseases and provided a bigger framework in which interlinked levels of relationships include molecules, organ systems, behaviour and social

organisation (Anderson, 1998). This framework allowed risk factors to work together in various combinations and also added the social dimension. How can what is known about the asymmetrical distribution of wealth and health be converted into managing health services? (Huntley et al., 2012) How can the burden of disease be measured? CIRS is the acronym for cumulative illness rating score. It calculates the morbidity burden by using severity gradings in 14 domains (Hudon et al., 2005). 'Aggregated diagnostic groups' (ADGs) stands for a management algorithm derived at Johns Hopkins University (University). It allows the morbidity burden to be quantified. It is applied to individuals and also used for 'population profiling'. 'Each ADG is a grouping of diagnosis codes that are similar in terms of severity and likelihood of persistence of the health condition over time'. The five dimensions are duration of the condition, severity of the condition, diagnostic certainty, aetiology of the condition and specialised care involvement. Variations on this theme are currently used in the NHS as a predictive modelling index. Higher scores trigger the generation of proactive care plans in an attempt to avoid hospital admissions.

## **WHAT IS KNOWN TO REDUCE THE COMORBIDITY BURDEN? WHAT WORKS?**

Managing activity limitation and participation restriction in people with comorbidities is a challenge not only for the practitioner–patient–relationship. Service coordination, environmental modification and continuity of care are important features (Vogeli et al., 2007). Service users in this situation have asked for support from a single coordinator of care, clear communication of individualised care plans and convenient access to providers (face to face or via telecommunication). The desirable interpersonal skills of these care providers were respect and an appreciation of the changing nature of needs (Bayliss et al., 2008). The Effective Practice and Organisation of Care (EPOC) Cochrane review group developed a taxonomy of intervention types. The classification addresses the provider organisation (e.g. case management as delivery method) and inter-service coordination tools like shared financial incentives to reach targets to facilitate effectiveness and organisational realignment. Other interventions focus on the patient (e.g. education, help for self-management) or the professional (e.g. education). A recent systematic review included ten RCTs and came to the conclusion: 'Multimorbidity is common in clinical practice and there is limited evidence supporting specific interventions'. The reviewers recommended specifying which specific outcome is the focus of the intervention (Smith Susan et al., 2012). Another review looked at a specific outcome – reduction in polypharmacy in older adults. It concluded that drug reviews by a pharmacist could identify inappropriate prescribing, but it was not clear whether this led to clinical improvements (Patterson Susan et al., 2012).

## **THE JOURNEY IS THE DESTINATION**

The biopsychosocial model is intended to provide an integrative umbrella for contributions from the biological, psychological and social sphere. It served originally as a counterargument against the biological reductionist model in the field of psychiatry. The sequence of the components suggests a hierarchy: 'Bio' comes first, followed by 'psycho' with 'social' being the appendix (McDaniel et al., 1989; Butler et al., 2004). Conversations about the medicolegal dimension of suffering, such as access to benefits, or litigation issues often reveal disputes about whose responsibility it is to do something about the unbearable status quo (Trilling and Jaber, 1993). The way the benefit system is set out may act as an institutional obstacle to getting better (Hadler, 1996). Making sense of body/mind/environment-interactions is a complicated task (Garcia-Moreno et al., 2006; Kirmayer et al., 2004). Doing something different, making shifts in behaviour, is an even bigger step. Acupuncture, with its embedded features of a caring therapeutic interaction and somatosensory stimulation, is an ideal vehicle for having these conversations, for asking the right questions

and for finding the right metaphor (Frank, 2004). Patient-centeredness and psychological flexibility are necessary requirements. The acupuncturist is, by the nature of the intervention, close to the physiological state of the patient. This closeness – the therapy being carried out in a close personal space – may be a help or a hindrance. Hands-on therapeutic relationships have the potential to be stalled in a state where the status quo is alleviated, but the benefit is insufficient. Chronic pain often has unhelpful behaviours as part of precipitating or perpetuating factors. Navigating the conceptual shift from a physical therapy to behavioural approaches is a challenge, and supervision may be needed to provide assistance.

## Where does acupuncture fit into the puzzle?

Like black boxes of different sizes, stacked together like Russian dolls, acupuncture, as a multimodal complex intervention, is enacted alongside other modalities for different purposes in different circumstances. This makes it difficult to answer the question about the place for acupuncture in primary care. The previous paragraphs concluded that the group most likely to receive acupuncture is the one which can be defined within more than one category – comorbidities, musculoskeletal pain with relevant psychosocial contributions to the pain experience. Acupuncture in the private sector deals with a different spectrum of conditions (and expectations) from acupuncture in the public sector (Robinson et al., 2012; Greenhalgh and Wessely, 2004; Thompson and Troester, 2002).

## CULTURES OF KNOWLEDGE AND CARE: PIPELINE AND GRASSROOTS

Acupuncture sits at the intersection of sometimes incommensurable healthcare sectors: the scientific bureaucracy, incorporated by policy making committees, the ‘swampy lowlands’ of primary care and the laying on of hands in the private sector. The practice of acupuncture is heavily influenced by its organisational context. The scope of practice, clinical governance structures and the demographic profile of the clients in private complementary and alternative medicine (CAM)-practice has very little in common with third-party-funded approaches via organisations representing the communities of taxpayers or insurance subscribers. A second difference exists between the macro-level of population-based policy making and the meso-level of managing what is possible within the given constraints. The organisational bodies regulating third-party funding rely on evidence generated by RCTs. The policy recommendations for acupuncture for common musculoskeletal conditions like low back pain, or osteoarthritis of the knee, vary depending on the interpretation of findings from meta-analyses. These recommendations have very little influence on service provision. A different and heterogeneous body of evidence from individual practices paints a picture of positive results stemming from integrating acupuncture into public funded primary care (Freedman, 2002; Robinson, 2012; Harborow and Ogden, 2004; Lindall, 1999; Ross, 2001; Ross et al., 1999; Johnson et al., 2008; Lim, 2010). Benefits for individual patients, and reductions in drug expenditure and referral rates, are common threads in these reports from the grassroots of primary care. There is a discrepancy in epistemic practices between the ‘pipeline’-approach of policymaking at high political levels, which sees knowledge being disseminated and implemented, and the grassroots-activities of local enthusiasts in their local environment which may be communicated within their communities of practice.

## CAPACITY, FLEXIBILITY, GENEROSITY

One major concern is the capacity to provide an acupuncture service for a given population, not just for a selected few. Given that there are benefits for individuals (improvement of at least threshold clinical importance) and care providers (shift in healthcare utilisation from drugs and

referrals to physical interventions) – how can this be sustained over time? How can acupuncture be delivered on an on-going basis like a repeat prescription, as intermittent reinforcement or maintenance therapy?

In practical terms it can be done within regular surgeries (e.g. at the end of the surgery) or in dedicated clinics. Size matters – having several rooms or at least couches available improves capacity. Simultaneous treatment on 3–4 couches can cater for ca. 20 patients in one session. Special consideration needs to be given to more vulnerable patients and situations, where either the behaviour of the patient affects the group or the group situation itself is an obstacle against better outcomes. Experiences from practices where acupuncture is part of the service spectrum suggest that delivering acupuncture as a nurse-led condition-specific service with flexible needling formulae in a group setting can provide the necessary capacity (Freedman and Richardson, 2008; Berkovitz et al., 2008). Qualitative research exploring the experience of receiving acupuncture in a group setting highlights the social dimension, which allows social learning and sharing stories to be a part of the intervention, though patients with complex histories or multiple complaints may need more privacy at times (Asprey et al., 2012). If acupuncture were to be integrated in routine primary care the service would have to address a key issue: How can interventions of acupuncture be delivered over time on an unlimited basis? The need is there, but it may not be legitimised by single disease categories like back pain or knee pain. Situations are more complex than that. The rise in therapeutic efficacy of biological treatments for diseases like cancer, the increase of survivorship from a variety of conditions in parallel with an increasing burden of medication and medication costs highlights the need for ‘adaptive work’, which includes techniques of how to look after oneself in the constraints of living with a long-term condition (Thygeson et al., 2010). Acupuncture as somatosensory stimulation aiming at neuromodulation seems to be a perfect candidate to be part of the therapeutic spectrum. The question remains about how the therapeutic relationship may be embedded in a network of chronic care management. One way to look at acupuncture is not at what it *does*, but at what it *does not* do: it does not have adverse effects like many drugs (gastrointestinal side effects, sedation, weight gain, renal failure) and the nonspecific effects of the intervention and the relationship may have additional benefits, which may make this intervention worthwhile. Worth how much, for whom, how long? What are the interests of the stakeholders in a funded relationship? The question is: with what economic, educational and governmental model can this be fitted into routine care? Care for chronic conditions with comorbidities attracts many promising labels: ‘Relationship-centred care’, ‘Goal-centred care’ to name just two (Frankel and Quill, 2005; Beach et al., 2006; Adams et al., 2004; Reuben and Tinetti, 2012). One key element is patient-involvement and community-engagement. Acupuncture is at the moment practised in niches and, on the whole, endorsed by the people at both ends of the needle. It relies on trust. It relies on preference and acceptance and is one of the therapies which cannot be done against the will of a patient. If there is an ‘opt in’ from all stakeholders in the relationship, it can be an interactive treatment modality which is worth pursuing. A lot depends on the organisational context. Trust and local knowledge may be the categories for finding particular ways to deal with a question which cannot be answered in general terms.

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# Acupuncture in dentistry

M.L.T. Thayer

## CHAPTER OUTLINE

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## Introduction

Acupuncture is a relatively recent development in dentistry. Because of the strong interventional approach that is required in dentistry (i.e. filling or extraction of teeth), the use of acupuncture follows a common theme in its application – enhancing the quality of treatment by facilitating conventional dental treatments, improving outcomes and reducing side effects or morbidity, rather than as a single treatment modality. Acupuncture is easily applied by dentists, or others, for dental treatment, with the majority of useful sites for stimulation lying on the head and neck. Within the UK, there has been significant interest in the technique, with a small number of dentists using acupuncture regularly as an aspect of their wider practice, and the technique is now taught within some postgraduate courses. Needling is typically undertaken within the surgery environment, with the expectation of rapid responses, but the use of indwelling needles for prolonged stimulus can also be most effective.

## Anatomy

The use of acupuncture in dentistry revolves around the trigeminal nerve, and to a lesser extent the glossopharyngeal and vagus nerves. The trigeminal nerve is the main sensory nerve to the orofacial structures, with some contribution from the cervical nerves, and has a motor root to the muscles of mastication, and a number of its branches carry 'hitch-hiking' autonomic fibres, or accessory sensory fibres, such as the chorda tympani. Prominent in management of dental issues is the control of pain, much of which is mediated through the terminal branches of the trigeminal – the superior alveolar nerves in the maxilla, and the inferior alveolar nerve in the mandible,

although referred pain to the orofacial and dental structures is a common problem, and is mediated through a range of other nerves, especially the upper cervical spinal nerves. The use of segmental acupuncture can feature prominently, with gate-mediated inhibition of sensory function for management of pain and dysaesthesias, but extrasegmental pathways may play a role in some cases.

However, muscular trigger points are a significant feature of orofacial pain for many cases that are not showing specific dental causes (i.e. a pulpitis or dental infection), and treatment options frequently target these trigger points. The muscles of mastication are the primary muscles involved, particularly at sites near to the origins and insertions of the muscles (Simons and Travell, 1998), as these muscles are frequently implicated in parafunctional (a dental term, meaning associated with altered and increased function) pain referred to dental structures. However, a common finding is referral of pain to the orofacial structures from the muscles of the neck and shoulder, particularly the sternocleidomastoid and trapezius, and these muscles should be assessed when considering the choice of acupuncture sites.

## Specific considerations in dental treatment

Needling is frequently directed towards treatment of muscular trigger points, and the *de qi* sensation is frequently experienced very strongly at these sites, which tends to reflect the sensitivity of these sites during examination. Whilst acupuncture will be helpful if *de qi* is not evident, the response seems much clearer when present and at some sites seems almost essential to be confident of an effective treatment. Clinical experience suggests that the size of sites varies, and whilst some may be only 0.5 mm across, others may be a large area perhaps 10 mm in diameter. Traditional needling is very effective in most cases, with most needle placement being within muscle at depths of 5–15 mm. Occasionally periosteal stimulation can be used, and in a few cases electroacupuncture may achieve a greater effect; however, this can prove problematic as this frequently stimulates the facial nerve, which appears to have a very low threshold for stimulus, and leads to contractions of the muscles of facial expression that some patients find very difficult to tolerate.

## The gag reflex

Perhaps the most important and dramatic application of acupuncture in dentistry is the management of the gag reflex. Dental care necessitates a significant number of interventional episodes in the oral cavity. Many patients find these episodes stressful, either as a result of anxiety related to dental care or as a result of the difficulties of the treatment itself. A very clear example of this is the gagging patient. The gag reflex is a normal protective reflex, but in some patients this is heightened to such a level that it interferes with the ability to accept routine dental care; indeed, for some patients the clinician may find difficulty even placing a dental mirror in the mouth. Such significant gagging prevents even satisfactory examination, including the use of intraoral radiographs, and thus impairs the ability to maintain adequate dental care. Delivery of significant amounts of any aspect of dental care in such an environment is extremely difficult, and outcomes are thus compromised. For some patients the ability to wear dentures is compromised, with significant functional and social impact.

Due to the significance of the gag reflex in dentistry, it has been the object of many differing treatment approaches over the years. Options range from simple distraction therapies to inhalational or intravenous sedation for more prolonged and complex treatments (Basi et al., 2004). Hypnosis has also been recommended as a modality. The key to deciding which approach to take lies in the level of anxiety of the patient: those with significant dental anxiety will require anxiety

management as the gag reflex is representing a defensive activity, at least in part, or is significantly exacerbated by the anxiety. Such patients respond very well to sedation but would respond poorly to acupuncture. On the other hand, those patients who have little anxiety, and perhaps simply present a physiologically sensitive gag reflex, are generally more suitable for acupuncture as an approach to control the reflex.

The use of acupuncture to control gagging in dentistry was suggested by Rosted (Rosted, 2000, 2004; Rosted et al., 2006) who recommended the use of Conception Vessel (CV) 24; Figure 38.1. Other sites reported as effective are PC6 (Lu et al., 2000) and ear points, either as a site lying between the outer helix and the tragus (Fiske and Dickenson, 2001) (sometimes known to UK dentists as the 'Fiske' point, Figure 38.2), or as ear points for tongue and relaxation combined.



**Figure 38.1** Point Conception Vessel 24 needled for control of gagging prior to dental treatment.

**Clinical approach.** CV24 (see Fig. 38.1) easily located on the midline at the centre of the base of the labiomental fold. The point is responsive to palpation, and clinical experience suggests it is no more than 0.5 mm in diameter. Needle depth is about 5–8 mm, and a strong *de qi* response is important. If this is not evident, adjustment of the needle is required. Paraesthesia of the local area is typically reported, that may extend into the lower incisor teeth, the lingual soft tissues and even the tip of the tongue in some cases. Use of the site is highly technique sensitive, but responses to needling are rapid, and in many cases the gag reflex is suppressed within 60 s with a high degree of reliability. In most patients the gag reflex is largely or completely suppressed, and for the rest, sensitivity is reduced. The needle is left in situ for the duration of treatment and removed on completion. Some patients see a very rapid return of the reflex, but most show a return over 20 min or so, and occasionally a patient reports longer-term reduction in sensitivity of the reflex.

A commonly perceived problem is that position of the needle may interfere with treatment, although *in practice* this is less of an issue than expected. More important is the impact of local anaesthesia, as anaesthesia affecting the labiomental area will block the effectiveness of the site.

CV24 will also respond to acupressure: firm fingertip pressure should be applied to the site for 60–90 s to suppress the reflex. This is not as effective as needling, but for those with needle phobia, this can prove very effective and may be easily employed. Patients may also be taught the technique to assist in their oral hygiene procedures, which are frequently compromised by the disruptive gag reflex.

The 'Fiske' ear point is not normally represented on acupuncture charts (see Fig. 38.2) and may have advantages over CV24 as this is remote from the mouth, and thus is not likely to interfere with access during treatment. It is also unaffected by routine dental local anaesthetic techniques.



**Figure 38.2** Ear point 'Fiske' for control of gagging.

This site may actually be a facial point rather than a true ear point and is considered as effective as CV24. It may be easier to use clinically as observation appears to demonstrate that the site is larger than CV24 and thus maybe somewhat less technique dependent. The site should be needled bilaterally, and it is also possible to double needle this site in order to increase the effect.

In practice there is no preference between the points, and in cases of significant gagging, three sites may be used – CV24 as well as bilateral ear sites. Classic ear points may also be used, but offer no advantage, and are more difficult to identify.

PC6 has long been used for the treatment of nausea and vomiting, and the link between nausea and gagging makes it a logical choice to employ this site. Conventional needling of PC6 will suppress the gag reflex compared to placebo (Lu *et al.*, 2000), but in some cases the effect may take 20 min to become evident.

In practice, PC6 is useful as it is remote from the mouth, but may be less practical in the busy clinic due to the slow onset of the effect. Needling with a short 0.20 mm diameter needle is effective, but quite uncomfortable for many patients. An alternative use for PC6 is to support of on-going control of the gag reflex for patients who are fitted with a new denture. Some struggle to adapt to the denture, and indwelling needles can be placed bilaterally at PC6 for 3–7 days to provide continuing control of the gag reflex, facilitating the process of adaption and frequently proving quite effective.

The great advantage of acupuncture over conventional treatments of gag reflex is a dramatic reduction in morbidity associated with treatment. Intravenous sedation is advocated as a management

tool, and in some severe cases general anaesthesia (such as for third molar surgery), but these carry significant impact on patients, and also limit access to care, especially in the acute situation. Acupuncture is rapid, easily applied with minimal training, and avoids these undesirable impacts.

## Dental anxiety

Dental anxiety may also form a significant barrier to the access of care and may also exacerbate gagging in some patients. Conventional practice may call for pharmacological approaches for management, but the relaxation that is commonly seen as a side effect of acupuncture treatments may be harnessed to manage mild to moderate dental anxiety in suitable patients (Rosted et al., 2010). Severe anxiety does not appear manageable, but acupuncture may be considered as a 'premedication', in combination with other behavioural management approaches, prior to other intervention in such cases.

**Clinical approach.** For mild to moderate dental anxiety, needling sites such as GV20 (with or without *Sishencong*) is typically recommended (Rosted, 2004) and may demonstrate a profound sedative effect. Identification of site GV20 seems to be the key to success. As with CV24, our experience is this appears very small, possibly only 0.5–1 mm in size, as clinically *de qui* is only identified at a specific point, with a relatively precise position (Shen et al., 2011) and is thus also very technique sensitive. Additional sites such as LI4 and LR3 may also be useful in enhancing the sedative effect. Acupuncture may be deployed as a supplement to other pharmacological sedative approaches – such as IV sedation – to enhance the quality of the anxiety control provided during the treatment episode.

However a small number of patients appear to demonstrate an inverse response to GV20 and become irritated by needling at the site.

Ear acupuncture may also be employed to provide anxiety control (Karst et al., 2007; Machalek-Sauberer et al., 2012) and may be applied for 24 or more hours prior to treatment sessions, using indwelling needles, applied to a number of sites bilaterally – either singly or in combination. Such an approach is quick, requires little surgery time, and might be delivered by a trained dental therapist or nurse.

## Dental pain

Pain is perhaps the most common significant presenting complaint in dental practice. Dental disease is common, and it is essential that the patient is fully assessed first to identify and eliminate any dental pathology that may be the cause of their pain, and only once this has been established should other causes for pain be considered. It should be remembered that dental pathology and other causes of orofacial pain may coexist.

Pain of dental origin may be considered in three areas – as a presenting (preoperative) complaint, as an intraoperative aspect of treatment, or as a postoperative consequence of treatment.

### PREOPERATIVE

Dental pain is typically due to diseases of the pulp, with pulpitis and periapical periodontitis being the two most commonly presenting diagnoses. The pain from these conditions is characteristic in nature, and frequently continuous, severe, disturbing sleep and may lead to distress. In such circumstances, whilst acupuncture may theoretically be used to aid analgesic prescribing, the only effective control for such pain is definitive dental treatment.

## INTRAOPERATIVE PAIN

Once a treatment need is established, acupuncture may offer opportunities to improve analgesic control during dental treatment. In clinical practice, difficulties with obtaining adequate anaesthesia during dental treatment are well documented, especially in the presence of acute inflammation when enhancement of analgesia would often be beneficial.

Some patients are enthusiastic to use acupuncture as an alternative to conventional local analgesia. Although there do appear to be some patients with whom it is possible to achieve some level of acupuncture analgesia – the problems of unreliability of the effect and delayed onset mean the use of the technique on its own is untenable in routine dental practice. A more promising application of acupuncture is in the enhancement of the effects of local analgesia; [Rosted and Bundgaard \(2003\)](#) demonstrated segmental acupuncture reduced onset time for local analgesic effect and improved reliability when using the inferior alveolar nerve block technique – a technique routinely employed by dentists and essential in the delivery of pain-free treatment in the mandible. This effect is likely to be a result of segmental (gate) inhibition of the inferior alveolar nerve by acupuncture.

**Clinical approach.** It is common to see areas of altered sensation in the orofacial structures during acupuncture to local points, with lingual paraesthesia being a common effect when needling ST7. As a consequence, segmental points such as those on the stomach meridian, the large intestine meridian and small intestine meridian are likely to be of use. SI19 is considered as a lead point, adding ST5, ST6 for the mandible, and ST3 and ST7 for the maxilla.

## POSTOPERATIVE PAIN

Postoperative dental pain is an area that has also received significant interest; it may result from surgical trauma (such as following extractions) or from delays in resolution of the acute inflammatory response of dental pathology, following interventions (such as root canal treatment). Studies have included simple acupuncture analgesia, or those where acupuncture is combined with oral analgesics. The general trend of evidence suggests that acupuncture is effective for postoperative dental pain control with a reduction in analgesic consumption and an increased time to analgesic consumption following surgery ([Lao et al., 1999](#); [Sun et al., 2008](#)).

**Clinical approach.** Analgesic points for the relief of postoperative pain may be either conventional body sites, including some segmental and some extrasegmental, or ear sites. Conventional sites would include points as outlined earlier, applied prior to the administration of local anaesthetic, in combination with such points as LI4, or LR3 bilaterally, with needles left in situ throughout the procedure.

Ear sites would include a target area – mandible or maxilla, along with analgesic points, in combination with *Shenmen*, and may be managed by use of indwelling needles for several days for a prolonged effect following discharge.

## Orofacial (non-dental) pain

### TEMPOROMANDIBULAR DISORDERS

Temporomandibular disorders (TMDs) are a common chronic pain condition, third in prevalence after headache and back pain ([Dworkin, 2011](#)) within dental practice, and TMDs represent the most commonly presenting pain of non-dental origin, although clinically significant symptoms are only reported by 2–3% of the population. Whilst the aetiology is mixed and

complex, it appears that the psychological axis of illness plays a significant role in the onset and maintenance of symptoms (Maixner et al., 2011). Patients presenting with TMDs may consume significant healthcare resources, with a range of interventions used including physiotherapy, cognitive behavioural therapy, occlusal splint therapy, pharmacological interventions such as non-steroidal anti-inflammatory drugs, antidepressants, and more recently botulinum toxin, as well as surgical interventions for joint derangement. Whilst TMDs are generally considered relatively benign and self-limiting, the symptoms may have significant impact on the patient, and in some cases severe functional deficit is evident. Treatments are often protracted, and outcomes can be variable.

Acupuncture offers an attractive and effective intervention for many patients presenting with certain aspects of TMDs (Fernández-Carnero et al., 2010; La Touche et al., 2010; List and Axelsson, 2010). Commonly presenting TMDs typically originate in the parafunction of the muscles of mastication, with, in some cases, an overlay of cervicofacial myogenic pain presenting a global pain picture. Patients typically present with pain or functional deficit of the temporomandibular joint (TMJ), and in some cases both. Those with myogenic pain are often good candidates for acupuncture (Shen et al., 2009), as with other musculoskeletal problems. Needling should be directed towards trigger points and tender zones in the muscles of mastication (Smith et al., 2006), especially those sites close to the origin and insertion of the masseter muscle (Simons and Travell, 1998), which correspond to traditional points ST 5, 6 and 7. In some cases muscular trigger points may be present in the centre of the body of the masseter muscle. GB2, on the posterior margin of masseter, is also often very significantly sensitive to palpation, and probably represents a muscular trigger point. The muscles should be palpated – bimanually where possible – to identify the sensitive sites, and needles inserted where active muscle trigger points or tender zones are identified. Typically the site ST6 is quite a large area, and the source of significant pain that is referred to distant structures and is commonly misdiagnosed as pain of dental origin (especially in relation to wisdom teeth). Where no dental pathology exists acupuncture might be considered as a diagnostic intervention in some cases, and if effective at reducing symptoms may help confirm a diagnosis of myogenic pain.

Point *Taiyang* (EX2) lies within the body of the anterior fibres of temporalis muscle and is also typically a site where symptoms of TMDs originate. Referral of pain from this site is a common component of headache, as an aspect of TMDs, and needling of this site is typically included in management of TMDs. Referral of pain originating from trigger points in the body of temporalis to dental structures – specifically the upper molars – is also a cause of misdiagnosis and inappropriate interventions.

**Clinical approach.** A typical approach for treating TMDs would therefore be to palpate the muscles of mastication to identify the most sensitive sites, which are typically ST5, ST6, ST7 and *Taiyang*. These may then be needled in an effort to control trigger point and parafunctional activity in the muscles of mastication. During such treatment, whilst classic gate control of pain may form an aspect of analgesia, it may well be that the primary aspect of acupuncture is creating environmental changes within the muscles. During parafunctional activity – classically nocturnal bruxism (grinding and clenching of the teeth) – areas of the muscles of mastication may become significantly ischaemic. In the vast majority of cases of TMD with myogenic pain, parafunctional activity is a prominent feature. Needling produces vasodilation within the affected areas, and thus reduces ischaemia, by enhancing oxygen delivery to the sites, leading to relief of pain. The change then may reduce muscle fibre activity, and return more normal function to the site and reduce pain by reducing tissue oxygen demands. This can be clinically recorded with a decrease in muscle tenderness on palpation, and an increase in mandibular opening in some cases. In support of this, thermographic imaging also shows an increase in muscle temperature, suggesting increased blood flow following interventions

to control bruxing (Barão et al., 2011). Treatment sessions *typically* require bilateral needling, although this is not always symmetrical. Responses are often (but not necessarily) apparent immediately, and overall patients show improvement in symptoms over the course of 4–5 treatment sessions. Extended courses of treatment are generally not required, and if symptom control is poor, this may indicate inadequate management of another aspect of the condition, particularly the psychological axis.

Long term control of parafunctional muscular activity is an essential aspect of treatment for TMDs. Without this, a return of symptoms is assured. Long term control requires the integration of acupuncture with other conventional therapies. As aetiological studies support the contention that stress plays a very significant part in the development and maintenance of TMDs and associated pain, acupuncture may be helpful in promoting relaxation. Needling should aim to support the treatment of pain from TMDs, reducing muscular tone and improve function. In addition, needling may be linked with the provision of an occlusal splint worn at night to enhance control of muscular activity. An alternative approach may be the use of botulinum toxin at trigger point sites to provide longer-term inhibition of muscle fibre activity. Indeed, acupuncture may act as a predictor to the potential effectiveness of botulinum toxin. However, whilst acupuncture may offer symptom control, it is important to recognise that for some cases psychological management such as cognitive behavioural therapy may also be necessary.

Mechanical problems within the TMJ are more difficult to manage. These may be divided into those causing clicking of the TMJ and those causing limitation of TMJ function. There may be evidence of both aspects. In some cases, acupuncture may offer benefits, but for those with obvious significant joint pathology or derangement (such as rheumatoid arthritis with joint condylar head destruction, or total dislocation of the meniscus), surgery is often the only appropriate intervention.

The most common mechanical problem is TMJ clicking – the primary issue in clicking is the anterior displacement of the TMJ meniscus. This should normally lie centrally in the joint over the head of the mandibular condyle, but during clicking it lies more anteriorly than normal. This is due to increased tone in the lateral pterygoid muscles, coupled with elongation of the retrodiscal ligaments. As the mouth opens, the disc becomes entrapped by the condyle, flexes, and then flattens – generating the click.

In practice acupuncture aims to reduce the tone in the lateral pterygoid muscles specifically, as well as tightening the retrodiscal ligaments. To this end, sites allowing needling of trigger points in the lateral pterygoid are most useful, and deep needling at ST7 will target this, along with more superficial needling directly in front of the TMJ itself. This is coupled with needling at SI19 – the needling seeking to create an inflammatory response in the ligament that then acts to ‘tighten’ the retrodiscal ligaments. Additional needling to reduce muscle tone in the adjacent muscles of mastication is also frequently necessary, as lateral pterygoid parafunction is rarely seen in isolation, and sites as described previously would be typical.

## DIAGNOSIS OF PAIN RELATED TO TMDs

Pain mapping within the structures of the head and neck can direct the clinician to the sites where undiagnosed pain is originating. The work of Simons and Travell (1998) is instrumental, and accurate within the orofacial structures. In cases with pain related to TMDs, for example, pain centred in the infraorbital area, with or without pain in the preauricular area or auditory canal can commonly be shown to originate from the lateral pterygoid muscle, and this may be treated by deep needling (30–35 mm) at ST7. Pain in the upper molar teeth may originate from temporalis muscle and is treated by needling of trigger points in the body of the muscle. The more challenging aspects of diagnosis come in identification of trigger points that refer from more distant sites

in the cervical muscles to the facial structures, particularly the sternocleidomastoid muscle, which produces some unexpected referral patterns within the facial structures.

## PERSISTENT IDIOPATHIC FACIAL PAIN AND ATYPICAL ODONTALGIA

Persistent idiopathic facial pain (formerly known as atypical facial pain) is a complex condition characterised by constant pain centred in the facial tissues (typically the maxillary or mandibular areas) which is unrelieved by a range of interventions from dental treatment to analgesics. Such patients are extremely difficult to treat conventionally, and current management regimes consider the condition more as a neuropathic pain. The mechanism is unexplained as yet, but onset typically follows multiple (dental) surgical interventions and may represent a form of trigeminal neuropathy.

Atypical odontalgia might be thought of as a variant of persistent idiopathic facial pain, although is normally considered a separate condition. The symptoms are similar, with persistent pain that is specifically centred in the dental tissues only. This condition probably also presents aspects of neuropathic pain, but the mechanism may be different from persistent idiopathic facial pain.

Oral dysaesthesia (or burning mouth syndrome) is a variant where patients complain of persistent burning or altered sensation within the oral soft tissues, most commonly the tongue, but it may affect any area of the oral soft tissues.

These non-odontogenic conditions probably all represent aspects of neuropathic pain. The major confounder with these conditions is the strong psychological overlay that is frequently evident in such cases.

Acupuncture may offer some relief (Scardina *et al.*, 2010) by the use of segmental approaches to reduce specific nerve sensitivity and in reducing concomitant muscle tenderness as a consequence of stress and anxiety-related muscle parafunctional activity, a common finding in such patients. There is a significant role for acupuncture as a diagnostic tool to identify and eliminate muscular trigger points that refer pain to the facial structures, mimicking pain of other origin.

**Clinical approach.** Responses are typically poor in the treatment of these conditions, but the condition most susceptible to treatment appears to be burning mouth syndrome, which may respond to a range of local approaches, such as CV24, CV23, stomach points and 'relaxation' points such as GV20. Strong stimulus generated at distant areas, such as LI4 or LR3, may also form key components to the management strategy in the form of raising general pain thresholds.

## TRIGEMINAL NEURALGIA

Trigeminal neuralgia (TN) is a specific condition characterised by brief, paroxysmal, stabbing electric shock-like pain in the distribution of one or more branches of the trigeminal nerve that has a characteristic small neurological trigger area in the soft tissues where the pain is initiated. Conventional treatment generally involves the use of anti-epileptic medication and, for some, surgery, such as microvascular decompression of the trigeminal ganglion, which appears generally very effective (Zakrzewska and Coakham, 2012). Acupuncture may be helpful in the treatment of TN (Rosted, 2004), acting either as a solitary treatment in mild cases, or as an adjunct when patients are already medicated, in some cases enhancing outcomes from conventional treatments and reducing side effects, or, more particularly, in patients who are unsuitable for surgery.

However, whilst the approach may be beneficial, some patients experience a temporary but troubling exacerbation of symptoms. Acupuncture should not be considered a ‘cure’ for TN, nor, in most cases, as replacement for conventional treatment, as the condition is generally persistent and may be intractable.

**Clinical approach.** Needling for TN takes two components: SI19 as a main point for all prescriptions, along with a number of local points in the distribution of the affected branch of the trigeminal nerve. Thus for a patient with mandibular branch symptoms, sites such as ST4, ST5, ST6 and ST7 would be ideal starting points, and for the maxillary branch, sites such as ST3, and ST4 or LI20 would be ideal. Stimulus is brief but may be increased depending upon responses. The use of distal points such as LI4 or LR3 would be dependent upon the case, but may be useful for increasing general pain thresholds, although there would be no segmental impact.

## SINUSITIS

Acute maxillary sinusitis may well present to the dentist simulating dental pain (Hegarty and Zakrzewska, 2011) that can be so intense as to lead to extraction of maxillary teeth. The floor of the sinus lies close to, or involves, the roots of the maxillary premolars and molars, and inflammation in the sinus may lead to irritation of the superior alveolar nerves running in the walls of the sinus, leading to dental pain. In such cases treatment with acupuncture should be directed to reduce secretions in the sinus and enhance pain thresholds. Sinusitis involving other sinuses may be much more significant and should be treated conventionally.

Chronic maxillary sinusitis generally presents less commonly to dentists but can sometimes be implicated in the diagnosis of dental pain. An alternative presentation for ‘chronic sinusitis’ is myogenic pain referred from lateral pterygoid muscle leading to patients presenting with facial pain, centred in the sinus region, despite a lack of apparent pathology. The pain referral pattern of this muscle is to the preauricular, TMJ, and infraorbital areas, and treatment of trigger points within the muscle will frequently relieve symptoms of ‘sinus’ pain.

**Clinical approach.** It is important to distinguish between sinus symptoms due to pathology (including dental pathology) and those due to myogenic pain. Symptoms of true sinusitis should be treated with local points ST3, SI18, *Yintang* (EX1), BL2 and LI20. Of these, ST3 is the most important. For significant pain, analgesia may be enhanced with distal points such as LI4, and LR3.

For those presenting with myogenic pain, deep needling of the body of lateral pterygoid at ST7 and just in front of its insertion onto the condylar head is usually effective in relieving symptoms. Distal points are not typically involved.

## HEADACHE

Headache has multifactorial origins, and careful investigation and diagnosis should be made prior to intervention. Chapter 24 deals with headache overall, but headache may present as an aspect of TMDs in some, but not all, patients. Acupuncture can be very effective in the treatment of headache (Linde et al., 2009a,b; Sun and Gan, 2008). A number of patients present to dentists having received extensive investigations, with no outcome, as the problem largely lies in functional changes in the muscles of the head and neck, rather than presenting a pathology. Headaches associated with TMDs are typically tension type headaches, with pain commonly felt in the frontotemporal position that may originate with trigger points in temporalis muscle.

However in some cases, headaches are centred in the cervical muscles, especially when presenting with generalised myogenic cervicofacial pain, with radiation to facial structures, as well as to the occipital and also temporal regions. Referral pathways are characteristic and follow the trigger point pain referral mapping of [Simons and Travell \(1998\)](#).

Careful palpation of the muscles of the head and neck may reveal a number of muscular trigger points. Trigger points typically form in trapezius and sternocleidomastoid muscles and present at GB20 and GB21, sites that commonly refer pain to the head and facial structures, and BL10 or BL11, or SI14–SI16. In the temporalis muscle, multiple trigger points may be present, or there may be a single site. Trigger points lie within the muscle along the temporal lines, frequently in the anterior fibres, and within the body of the muscle, and are frequently associated with headache, both tension and migrainous.

From a dental point of view, patients with headache or migraine, especially when related to TMDs, may respond well to acupuncture, but may also benefit from the provision of an occlusal splint as for other TMDs in order to maintain changes induced in the muscles by needling of trigger points.

**Clinical approach.** It is important to identify first the sites of origin of the patient’s pain. Prescription for headache may then take a layered approach with each layer treating a specific aspect of the muscular origin of the pain. Typical sites for needling are mainly local trigger points within the temporalis, such as GB1–GB8, *Taiyang*, along with distal points such as LI4 and LR3, to enhance overall pain thresholds and promote relaxation.

Headaches with a strong cervical component should be treated using a combination of points within the temporalis, together with those within the cervical muscles, the most important of which are GB20 and GB21, but in combination with other sites such as SI14 or SI15, BL10 or BL11 and local trigger points ([Table 38.1](#)).

TABLE 38.1 ■ Treatment guide for dental conditions

Condition	Cause	Muscles involved	Needle sites	Treatment duration
Gag reflex	Physiological reflex	N/A	CV24 and/or ear site	For entire treatment session. Ear sites bilateral and double needled as required
			PC6	5–7 days for denture adaption. Bilateral
Dental anxiety	Psychological	N/A	GV20 and EX6 Add LI4 if required Consider auricular approaches	For duration of treatment session May be applied preoperatively
Dental pain intraoperative	Pathology or surgery	N/A	SI19, with ST5, ST6 for mandible, or ST3, ST4, ST7 for maxilla	Apply several minutes preoperatively to enhance local anaesthesia Unilateral to area treated
Dental pain postoperative	Surgical trauma	N/A	SI19, with ST5, ST6 for mandible, or ST3, or ST4 and ST7 for maxilla	Apply from commencing treatment and maintain until treatment complete. Unilateral or bilateral

*Continued on following page*

TABLE 38.1 ■ Treatment guide for dental conditions (continued)

Condition	Cause	Muscles involved	Needle sites	Treatment duration
TMD				
1. Myogenic pain	Parafunctional muscle activity, and trigger point formation	1. Masseter 2. Lateral pterygoid 3. Temporalis 4. Trapezius	1. ST5, ST6, ST7, ST8, GB2 2. ST7 deep 3. EX2, ST7, GB8 plus trigger points 4. GB20, GB21	10–20 min. Unilateral or bilateral. Sites dependent upon palpation and previous response Link with conventional therapy
2. Clicking	Parafunctional muscle activity	Lateral pterygoid	ST7 deep with SI19, and superficial needling anterior to condylar neck	Identify other muscles of mastication involved and treat accordingly
Trigeminal neuralgia	Neurological	N/A	SI19 master point Add: First branch – EX1, EX2, ST8, GB14 or BL8 Second Branch – ST3, or ST4, or ST7, LI20 Third Branch – ST4, ST5 or ST6, ST7, CV24 if needed	Brief stimulus. Only treat affected area
Sinusitis	Infective	N/A	ST3, ST7, SI18, LI20, EX1, BL2	Only treat affected side Eliminate referral of myogenic pain
Headache	Multifactorial. Specific-myogenic related to TMD	1. Masseter 2. Lateral pterygoid 3. Temporalis 4. Trapezius	1. ST5, ST6, ST7, ST8, GB2 2. ST7 deep 3. EX2, ST7, GB8 plus trigger points 4. GB20, GB21, BL10, BL11, SI14, SI15, plus trigger points	10–20 min. Unilateral or bilateral. Sites dependent upon palpation and previous response Eliminate other causes of headache

## Concluding comments

Acupuncture is a useful technique in dentistry to supplement conventional treatments, either in facilitating treatment, or linking with conventional treatments to enhance the outcomes. It is important to distinguish between pain of dental origin, and that of muscular origin, as treatments will have different aims. As a consequence, acupuncture in dentistry relies heavily upon segmental effects, along with trigger point techniques.

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# Acupuncture in veterinary medicine

S. Lindley

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## Introduction

It has often been said that acupuncture has been practised on the veterinary species for as long as it has been practised on humans. There are apocryphal tales of lame horses becoming sound during battle after being wounded by arrows, leading to the speculation that piercing of the skin could have therapeutic properties. This seems a little unlikely for practical if not logical reasons. More likely, once animals became domesticated, and of material and financial value to their owners, those owners would look for ways of healing diseases that would lead to ill thrift (i.e. poor body condition and an appearance of not thriving) and dysfunction. Moreover it would be logical to use some of the same techniques on animals that they used to treat their own pain and other symptoms. We know that acupuncture and acupuncture-like stimuli have arisen in cultures all over the world (Bivins, 2000), not just in China, so it would seem likely that animal owners used these same techniques on animals regardless of whether animals 'fitted' into traditional concepts of meridian theory, the five phases or yin-yang approach to disease and well being.

## CURRENT PRACTICE

Current veterinary undergraduate training does not include acupuncture except for a few specialist lectures and the potential for observing the practice in chronic pain clinics where they exist at veterinary schools. However, more veterinarians are becoming interested in acupuncture as companion animals (dogs, cats, horses) live longer and consequently live with chronic pain and disease for a greater proportion of their lives. Livestock species such as cattle, sheep and pigs are less popular targets for acupuncture today because the financial margins in farming are slim and the relative cost of repeated, time-consuming treatment for one animal is not viable.

Acupuncture is sometimes asked for by so-called ‘hobby’ farmers where their livestock are few in number and of emotional rather than financial importance. Veterinary acupuncture is also used in practices that treat domestic fowl (hens, ducks, geese) and exotic animals, including birds such as parrots; ‘small furies’, such as rabbits, rats and guinea pigs; and even reptiles. Actual numbers of veterinarians practising acupuncture is unknown, but around 1000 have been taught (either through a traditional Chinese Medicine route or a ‘Western, scientific,’ approach, predominantly the latter) and there now exists a university accredited certification process in Western Veterinary Acupuncture and Chronic Pain Management.

Veterinary acupuncture is often of interest to medical acupuncturists for a variety of reasons. The novelty of considering the application of techniques, familiar to human medicine seems to intrigue a medical audience. The first question usually asked in regard to the use of veterinary acupuncture is whether or not the patients can be kept still for long enough to insert the needles. After a bit more consideration the interest commonly crystallises into the assumption:

‘If it works in animals, acupuncture cannot be just ‘placebo’.

There are difficulties with both parts of this statement. The first is the all important ‘if it works’. There is of course a huge literature on positive laboratory studies on the effects of acupuncture in animals and largely anecdotal evidence for its clinical effects in veterinary practice, which is mainly based on extrapolation from the known effects of acupuncture in humans (Lindley and Cummings, 2006). There is still a paucity of good quality clinical trials to prove effectiveness (when compared with a standard treatment), or efficacy (against sham), in any of the conditions for which acupuncture is frequently used in veterinary practice. A systemic review in 2006 (Habacher et al., 2006) concluded that there was little evidence for the effectiveness of acupuncture in veterinary medicine, but that review included only 14 randomised controlled trials and 17 controlled trials. Many of these were of poor quality, often using needling as a ‘sham’ technique, and they covered a wide range of conditions, many of which one would not usually consider as indications for acupuncture, e.g. diarrhoea in piglets (because there are usually more specific treatments), although this condition and induced Cushing’s disease in dogs were deemed worthy of further study. The latter was especially bizarre as it actually described induced hypoadrenocorticism rather than hyperadrenocorticism (Lin et al., 1991). One of the major problems with all veterinary research is small sample size, often no more than twenty patients in total. Improving on this shortcoming is problematic even by using crossover studies because the difficulties of ‘washout periods’ when using acupuncture. An additional challenge to veterinary research is the multiplicity and diversity of species, almost certainly with different responses to acupuncture.

The other challenge for the ‘if it works’ part of the assumption is regulation, particularly in the UK. In a UK clinical trial on animals, one must show an ‘intention to treat’ in order for the trial to be considered ethical (this is not the same as the statistical analysis referred to as ITT). Therefore clinical trials are likely to be effectiveness studies – comparing acupuncture with a standard treatment or adding acupuncture to a standard treatment and comparing it with the standard alone. Once one embarks on efficacy studies or compares acupuncture with no intervention at all, there is an absence of intention to treat so the trial becomes experimental, with all the Home Office regulations that this, quite rightly, entails. The point here is that animals cannot choose to enter a trial in the knowledge that they may be in a ‘sham’ or control group. It is not an issue of better protection for animals but of absence of choice that makes animals more vulnerable than humans.

Then there is the problem of defining ‘works’. In conditions other than pain, there may be clear and definable outcome measures, but there are still difficulties with validated pain scales for the veterinary species. There are some validated acute pain scales (Holton et al., 2001) and one long ‘quality of life’ scale (Wiseman-Orr et al., 2004, 2006), which is validated for canine

orthopaedic patients and is in the process of being made more concise, but a reliable, validated chronic pain scale is still elusive. Acupuncture is most frequently used for chronic pain problems in companion animals, and chronic pain is the most difficult kind of pain to assess, therefore deciding whether acupuncture 'works' will depend to some extent on the experimenter's definition of success.

As if all that were not tricky enough, there remains the issue of 'placebo'. Literally translated as 'pleasing the patient' we now know that it is so much more than this and exists as a real and often potent neurophysiological effect that can be targeted and blocked. It is known that animals have 'placebo' responses, and these have to be accounted for in any clinical study. So, even if the first part of the assumption were established (that acupuncture works in animals) the second is not unless placebo is accounted for. To add to the difficulties, there is also the influence of owner expectation, which includes their confidence in the practitioner and in the technique – often called 'proxy placebo'. It would be unlikely that these influences could alter very 'hard' outcome measures (rate of wound healing, blood flow measured by Doppler ultrasound scanning, for example), but, given that pain in animals is often measured at least in part by changes in behaviour, a change in attitude of the owner towards their pet can alter behaviour and therefore the perceived outcome of an intervention. For example, frequent sympathetic attentions and worry over a pet may reinforce behaviours and postures that are associated with feeling unwell or in pain. More positive body language and an upbeat approach from the owner can alter which of the pet's behaviours are rewarded and shift the pet's behaviour towards the more positive.

So, from a rigorously scientific standpoint, in terms of an evidence-based approach to acupuncture in the veterinary species, one is left with what experimental animal studies demonstrate, which is quite a lot. One might argue about extrapolating their relevance to humans, but clearly there is likely to be direct clinical relevance for the animal species in which they are conducted as much as there ever is for an artificially created pathological condition compared with a naturally occurring disease.

## Clinical approach in veterinary acupuncture

The principles of acupuncture treatment and treatment methods are broadly the same for the veterinary species as they are for humans. A history taken from the owner will be followed by thorough examination of the patient and, if musculoskeletal pain is the problem, the gait observed. The needles are placed as close as possible to the source of pain without making the pain worse. More needles are often used in animals than in humans for two main reasons: commonly the patients presented have had pain for a long time and the tenderness shown on palpation is widespread; secondly, although pain can be discerned on palpation to be worse in some areas than others, the patient cannot verbalise which painful responses are relevant to their suffering and they cannot of course describe the pain of a myofascial trigger point as 'their pain.' There is, therefore, a certain amount of hedging of one's bets in needle placement, with up to 15 or more needles commonly used at each session where patients have chronic pain or multiple pathologies.

Treatments for generalised conditions such as atopy or nausea tend to use points that are easy to stimulate strongly while being tolerated by the patient. In animals these tend to be upper limb points and points in the back.

## STIMULATION OF NEEDLES AND 'DOSAGE'

Some veterinary acupuncturists take the view that it is not necessary to stimulate the needles manually because animals usually move about more than do human patients and therefore 'self stimulate.' However, most clinicians will use lift and thrust or rotation techniques, adjusting the

frequency of stimulation in response to the animal's immediate reaction to the sensation and their clinical response to the treatment. Treatment times can be as short as 20s or as long as 30 min, the latter being especially relevant when electroacupuncture (EA) is used to alleviate severe pain.

EA is used in the veterinary species when the patient needs more potent stimulation, i.e. if dry needling does not appear to be having an effect even though acupuncture is indicated or as the pathological process progresses so that there is effectively more with which the acupuncture stimulus has to compete. The frequencies used vary between practitioners, but this author tends to use dense dispersed programmes of 2 and 100 Hz or 2 and 80 Hz unless the evidence suggests otherwise for a particular condition.

## EVALUATION OF ACUPUNCTURE TREATMENT

Pain scores and quality of life scores are available for some species, although their validation is usually limited to a certain group of animals, e.g. canine orthopaedic patients. They are reliant on good owner observation and to some extent on the assessment of behavioural changes in the animal.

Animals appear to be overall better responders to acupuncture than do human patients, but there are still some apparent 'non-responders.' In these cases, the possibility must be acknowledged that the original diagnosis may have been faulty and that acupuncture was not an appropriate technique to use for these particular signs or in this particular patient. Another possibility is that response is determined genetically. In larger species such as the horse, where a definitive diagnosis can come at an even higher price than it does with the smaller companion animals, there is a temptation amongst owners to use therapies such as acupuncture, and those with less credible pedigrees, as an alternative to spending money on diagnosis. This makes it more likely that treatment will be inappropriate.

## Veterinary acupuncture: a pragmatic approach

### ACUTE AND CHRONIC PAIN IN COMPANION ANIMALS

Most veterinary surgeons enrolling on a Western scientific acupuncture course state that they would like to learn acupuncture in order to help their chronic pain patients. Chronic pain medicine is in its infancy in veterinary medicine; the kind of chronic pain clinic familiar to human medicine has been rare (but is rapidly becoming more common), and protocols and approach are far from standardised. Yet, owners and vets are becoming increasingly aware of the presence of chronic pain in animals and its implications such as reduced quality of life for the patient. As a result, unlicensed analgesics are now being used more widely in companion animals because licensed medications are limited largely to non-steroidal anti-inflammatory drugs (NSAIDs). There is an increasing awareness that more can and should be done for our chronic pain patients. Increasingly, many owners worry about the potential side effects of medication and search for safer alternative or adjunctive therapies. Therefore, although there is still little clinical data to support its use, it appears that the most frequent indication for the use of acupuncture in the veterinary species is chronic pain.

### The treatment of acute pain

There is a misguided belief amongst some veterinarians that pain must be chronic before it can be treated by acupuncture. There is no reason why this should be so, and most of the experimental studies demonstrating analgesic effects and mechanisms have been done on animal models of acute pain. The veterinary profession does have ready access to, and often

uses, potent analgesics such as the opiates and multimodal techniques such as morphine-lidocaine and ketamine combinations for acute pain (where it can be recognised) and for perioperative analgesia. There may be a perception that acute pain can be well managed compared with chronic pain and that there is no need for adjunctive therapy. Unfortunately, even acute pain can be hard to recognise in animals (because sometimes the animal just does nothing – vocalisation does not occur as frequently as one might expect), and under-treatment of acute pain is still common.

There are studies on the use of acupuncture perioperatively in dogs: a small ( $n=30$ ) study comparing dogs undergoing mastectomy given morphine, or EA, or a sham treatment (needling into 'non-points' with no stimulation) showed no difference between the morphine and real or sham acupuncture groups, but rescue analgesia was needed less frequently after EA (Gakiya *et al.*, 2011).

A study ( $n=12$ ) comparing the use of EA with butorphanol for ovariohysterectomy showed higher blood concentrations of beta endorphins, lower isoflurane requirement (end-tidal measurement) during the surgery, and less rescue analgesia administered with the acupuncture group (Gropetti *et al.*, 2011).

Cassu *et al.* (2012) looked at the postoperative analgesia achieved in dogs undergoing ovariohysterectomy ( $n=18$ ) by either EA bilaterally in the hindlimbs, or by needles placed longitudinally on either side of the skin incision parallel to the linea alba; or by both limb EA and skin acupuncture. The study demonstrated that EA into limb muscles achieved better analgesia than two needles under the skin with no stimulation, but although the authors' claimed that the technique could be used in practice, the degree of analgesia achieved (analgesia was inadequate in one third of the dogs) was not sufficient to argue for EA as a sole analgesic for this kind of surgery.

Acupuncture appears to be a useful adjunct to acute analgesia. In this author's experience at Glasgow University Veterinary School, acupuncture has occasionally been the only, or the additional, intervention that appears to have reduced acute pain sufficiently to allow a distressed patient to sleep.

The delivery of acute analgesia to a horse, except when sedated, is challenging since acute pain often produces a very marked response in horses (especially those with abdominal pain) with kicking, bucking, rolling, sweating, stamping and other behaviours that would make the delivery, if not the maintenance, of the technique hazardous. But for less severe presentations it may be feasible and useful. Point selection would depend on the condition; segmental, paraspinal points would be chosen for visceral conditions and local needling, including trigger points, for musculoskeletal problems.

## Chronic pain conditions

Osteoarthritis is a common condition in dogs and cats. In dogs, the condition is usually secondary (i.e. as a result of dysplastic joints and poor conformation) and, as a result, occurs earlier in the animal's life, although it may not always cause problems until the patient is older. Therefore it is not unusual for owners to be faced with the prospect of managing a potentially debilitating condition, which often presents in multiple joints, when the dog is under a year of age.

Cats develop primary osteoarthritis, i.e. as a result of 'wear and tear', and therefore it is mainly a disease of older cats (over 8 years, with a rapid increase in incidence over 12 years of age, Godfrey, 2005; Clarke and Bennett, 2006). But pain in cats is even more difficult to recognise than in dogs, and so many cats are left to 'cope' with osteoarthritis whilst their owners just assume that they are getting old.

Osteoarthritis in dogs and cats appears to be associated with secondary myofascial pain in the muscles associated with the affected joints, but also very commonly in other muscles that are strained by the animal's attempts to shift their weight in order to ease the joint pain. Because

it is so difficult to recognise pain in animals, these patients probably spend longer in pain and adjusting to that pain before they get help. It is not surprising therefore that there is widespread myofascial pain and often chronic pain changes such as hyperalgesia and allodynia, indicating central sensitisation, in many companion animal patients. Since acupuncture is arguably one of the best techniques for dealing with myofascial pain syndrome in humans, it would be expected (and is frequently seen) that these patients often do well as a result of acupuncture treatment after the failure of even quite potent analgesics. One of the problems in assessing any intervention is that for a given diagnosis of arthritis, there is a range of painful conditions, from myofascial pain to central sensitisation, that may actually be under-treatment, and these would be usually treated by different approaches.

That is just one of the limitations in interpreting the following two (arguably most rigorous) studies relating to acupuncture for canine osteoarthritis (OA), which are negative. The first ( $n=38$ ) involved testing gold bead implants at acupuncture points for OA hip by comparing gold beads inserted through a 14 g needle around the hip (verum group) with 14 g needles alone inserted around the hip (control group) (Hielm-Bjorkman et al., 2001). Both groups improved, but there was no difference between the groups. As the authors themselves point out, the study was done in the summer and all owners were given general advice regarding management of OA (i.e. one would have expected the dogs to improve anyway). Essentially the difference between the two groups was needle trauma in the hip girdle plus gold beads, compared with needle trauma in the hip girdle. Whatever relationship this technique bears to acupuncture, it is not acupuncture.

A study on elbow OA ( $n=9$ , Kapatkin et al., 2006) using force plate assessments and pain scores is of reasonable design and negative. However, the authors themselves discuss numerous possible confounding factors, and additional factors have been discussed earlier. This study was a crossover design comparing EA once weekly for 3 weeks with sham EA. What would have been interesting to know is whether these same dogs would have had improved scores following potent pharmacological analgesia.

As is the case with humans, dogs and cats are living much longer than they did previously. Pets are not dying or being euthanased so commonly with sudden or untreatable organ failures, or even cancer. They are therefore subject to the effects of pain for much longer. It follows that veterinary geriatric medicine must include the treatment of chronic pain and muscle weakness that occurs as a result of the muscles not being used properly because of musculoskeletal dysfunction.

Horses are prone to bony, tendinous, ligamentous and muscular pain. Because the strains that are put on their musculoskeletal systems are potentially profound, and because clinical investigations are by their nature involved and expensive (everything being on a larger scale), they are candidates for all sorts of pain treatments from the orthodox to the apparently bizarre, such as a single knuckle jab in the ribs from a particular “back” man’. Acupuncture is frequently and apparently successfully used for chronic pain in horses of all types, from children’s ponies through to valuable race and performance horses. One major advantage of acupuncture and other non-pharmaceutical treatments is that there is no ‘withdrawal period,’ as there may be for a pharmaceutical agent, so horses would be allowed to compete with no restriction after treatment.

## DERMATOLOGY

Dermatological conditions in the veterinary species are as challenging, potentially frustrating and every bit as distressing as they are in human medicine. The extent and effect of pruritus and self-trauma that can occur in an atopic animal is arguably a more serious welfare concern than are some painful conditions.

The most common dermatological condition in dogs that manifests as self-mutilation is ‘acral lick dermatitis’. This is a granulomatous lesion caused by excessive and compulsive

licking on the distal part of any limb, commonly over or near the carpus or hock (ankle) joints (Veith, 1986; Walton, 1986). There are multiple aetiologies: tumour; non-healing injury; neuroma; local or referred arthritic or muscular pain; atopy; infection. It is therefore rather startling to encounter numerous practitioners who claim great success with this condition by using acupuncture, depending on the underlying cause. The techniques vary from a simple 'surround the dragon' technique to needling away from the site further up the limb. The 'surrounding' approach should optimise wound healing, but the point about these lesions is that, more often than not, if one can stop the patient licking the wound (usually by the use of cone shaped collars that stop the dog reaching the site) it will heal without further treatment, i.e. failure of healing does not appear to be the issue in most cases. The most common breeds with this condition are large breed dogs such as the labrador, and these dogs also frequently suffer from osteoarthritis, so it is possible that the majority of successes are due to simply treating the pain in the limb.

Cats also suffer from self-mutilation problems – these can be anything from overgrooming to active self injury. Sometimes these are truly psychogenic and in response to an inappropriate environment; sometimes they are the result of ectoparasite infestation; and sometimes the result of pain. Cats tend to be less likely than dogs to display neurological signs as a result of lumbar disc prolapse and so may 'just' present with pain. As previously mentioned they also commonly suffer with the pain of OA. Unfortunately for the clinician, this pain may be manifested as aggression; or anxiety; or withdrawal; or inappropriate toileting; or self-mutilation. Such behavioural abnormalities are not pathognomonic for any specific condition, and a careful history is required to establish, if possible, the cause. Cats appear to respond very well to acupuncture and treatment of chronic disc pain and osteoarthritis can be successful, but the starting point of self-mutilation as a sign is a long way from the decision to try needling as a therapy.

Atopic dogs represent a significant proportion of dermatological cases. Standard treatments range from identifying and minimising, where possible, the allergens involved; management with anti-histamines and corticosteroids; immunosuppressants such as cyclosporine; and autogenous vaccines. Some patients fail to respond to any of these or have significant, adverse side effects. It appears that a few dogs respond extremely well to acupuncture for this condition, and it would be useful to find out whether this is a true phenomenon and, if so, what proportion of atopic patients respond. It is certainly the case that some of those that respond well to acupuncture for a painful condition and that have concurrent atopy have no change in their atopic signs, so a response to acupuncture in general is not sufficient to give a good prognosis for the treatment of atopy.

Canine otitis externa is a problematic condition that can occur as an isolated condition or as part of generalised skin disease. Sánchez-Araujo and Puchi (1997) have demonstrated a useful effect of acupuncture, using dermatomal and auricular points, on this condition in the short term and in a 1-year follow-up study (Sánchez-Araujo and Puchi, 2011).

## Wound healing

Cats and dogs frequently suffer from traumatic injuries and have surgical wounds that may break down due to failure to rest or infection. These wounds are often left to heal by second intention and the patient required to wear an 'Elizabethan collar,' or large plastic cone, over their heads to try to prevent them continually licking the wound. Anyone who has lived with a large or boisterous dog battering legs and furniture with these objects would welcome the prospect of speeding up the wound healing process. The clinical and experimental evidence for using acupuncture to achieve this would suggest it is well worth a try (Lundeberg et al., 1988; Jansen et al., 1989a,b), and the author has used it with success in a number of cases.

Horses tend to suffer from 'proud flesh,' or excessive granulation tissue, after acquiring wounds in the lower limb. The problem is common and requires intensive treatments, dressings and

sometimes ‘seeding’ of skin grafts in order to assist healing. Acupuncture has been shown to optimise healing and so should be a useful technique in these circumstances, although there are no reports to date. Given that the wounds require regular examination and dressing it would be simple to add a ‘surround the dragon’ needling session to the treatment.

## NEUROLOGICAL CONDITIONS

The main application for acupuncture in neurological conditions is in the management of pain. Disc prolapse, nerve root irritation and foraminal stenosis are conditions that are commonly accompanied by secondary myofascial pain and central sensitisation.

Some studies appear to show good results for the treatment of disc disease in dogs and would be worthwhile following up given the prevalence of the condition and its impact on welfare. [Han et al. \(2010\)](#) reported a retrospective study of 80 dogs with thoracolumbar intervertebral disc herniation and paraplegia (deep pain perception intact). Thirty-seven of the dogs had been treated with corticosteroid and 43 with corticosteroid, EA and acupuncture. EA was to GV7 and GV1–GV2 at 2–15 Hz for 25–30 min; acupuncture was to bladder points local to the lesion and to hindlimb points GB30, GB34 and ST36. The group receiving EA and acupuncture plus corticosteroid appeared to recover more quickly and relapse less frequently than the group receiving corticosteroid alone. Another study of 40 dogs with intervertebral disc disease ([Joaquim et al., 2010](#)) compared decompressive surgery with EA and with decompressive surgery followed by EA. The study showed a better result for EA alone than for either surgery alone or surgery plus EA, although the latter was better than surgery alone. This was both a retrospective trial and prospective clinical study with the retrospective part drawn from the last ten dogs to undergo decompressive surgery.

Although one would not expect the signs of direct nerve involvement (inferred by jumping/starting type behaviours) to be amenable to acupuncture, they often seem to be. This is most likely to be because these signs are very crude indicators of the type of pain with which one is dealing and what looks to be true neuropathic pain may be in fact be nociceptive or mixed in its origins. In conditions where the both the signs and the results of imaging strongly suggest the pain is neuropathic, acupuncture predictably fails to improve the major signs. The most obvious of these is Chiari syringomyelia (CSM, a canine variant on Arnold–Chiari malformation in man) where the fluid filled syrinx and herniation of the cerebellum through the foramen magnum leads to compulsive ‘phantom’ scratching of the neck and sudden bouts of screaming. In contrast, acupuncture is often very helpful in reducing the signs of depression and discomfort arising from secondary myofascial pain (and often concurrent pathologies such as OA and disc disease), but, whilst the dog will be happier overall, the frequency and severity of the scratching and screaming will usually not change.

## Wobbler syndrome

This condition occurs in Dobermann and Great Dane dogs, but also in horses, and involves abnormalities of the cervical spine resulting primarily in hindlimb ataxia. A study of 40 dogs ([Sumano et al., 2000](#)), in which 125 Hz EA was used on ten acupuncture points (including local to the neck) every other day, suggests further clinical studies on this condition would be merited.

## URINARY TRACT PROBLEMS

Cystitis is primarily a chronic problem in the cat and the cause of significant suffering. Dogs do present with cystitis and occasionally with refractory presentations such as follicular cystitis, but generally speaking canine cystitis is well managed by short courses of antibiotics and pain relief. The feline patient is prone to a number of conditions of the lower urinary tract, and there are multiple factors

at work; diet; not drinking enough water (often because the water bowl is placed too close to the feeding bowl); inactivity leading to less frequent urination; calculus formation and the great catch-all 'stress' (Westropp and Buffington, 2004). The most difficult form of cystitis to treat is idiopathic cystitis which is often sterile, recurrent and commonly triggered predictably by certain events in the cat's life (trip to the veterinary clinic; visitors at home; a new piece of furniture in the house).

Cats are very susceptible to changes in what is known as their 'core territory' (that space, usually the house, in which they expect to feel secure and have access to their resources). Whilst this space may look nice to the owner, it is frequently far from cat friendly and many cats live their lives on a knife-edge of coping. When they fail to cope it can trigger a number of physical and behavioural problems. Idiopathic cystitis is a complex disease and optimising the core territory is one useful way of tackling it (Buffington et al., 2006), but acupuncture could be helpful in a number of ways as long as the very act of being transported to the clinic and being given acupuncture is not in itself too stressful. Acupuncture at the time of an attack could provide pain relief and mild anxiolysis.

Some cats that suffer from cystitis have concurrent back pain, and it has been found in some cases that treatment of the back pain reduces the frequency and severity of attacks. There could be a number of reasons for this: the back pain could be the stressor; the back pain could arise secondary to the pain of the cystitis attacks; treating the back pain gives a segmental treatment to the bladder. It has also been found that these cats appear to be in the equivalent of a chronic pain state, at least in terms of the way their bladders respond to even normal urine. It should be at least theoretically possible to 'wind down' this state with repeated doses of acupuncture.

## Urinary incontinence

Urinary incontinence is usually a problem of the canine patient. The female dog often presents with incontinence some time after routine ovariohysterectomy (neutering). This incontinence is caused by a number of factors including a loss of oestrogenic effect on the physiological bladder sphincter (so-called sphincter mechanism incompetence, Holt and Thrusfield, 1993), combined with or exacerbated by in some cases the bladder moving from an intra-abdominal to a intrapelvic position (because of the absence of the uterus) where the pressure on the bladder wall is greater than when in its intra-abdominal position. In some cases the problem is caused as a direct complication of surgery, and in some cases there is a congenital ectopic ureter.

It should seem, from a review of the neurophysiological effects of acupuncture, that it would be unlikely to have much of a positive effect on any of these causes of incontinence, although it may just be possible to have an effect on the sphincter mechanism given that it is not all oestrogen driven. Yet it is often reported that acupuncture can have an effect on incontinence, and these reports seem at odds with the pathophysiology described. However, both male and female dogs can present with incontinence and concurrent lumbar pain. When the lumbar pain is treated, conventionally or with acupuncture, the incontinence resolves. Since lumbar pain is common and the 'traditional points' to treat incontinence include points along the inner bladder line in longissimus muscles (which are the same points found to be painful and needled when treating back pain), it seems likely that incontinence is reported to have been 'cured' as a secondary effect of treating this pain. It would seem logical therefore to target that population of dogs that present with lumbar pain and incontinence rather than those proven to have sphincter mechanism incompetence/intrapelvic bladder and no palpable back pain.

## GASTROINTESTINAL CONDITIONS

Megacolon is a condition of cats whereby the function of the colon is impaired and significant constipation results. This is a functional condition and appears to be amenable to acupuncture treatment. Segmental needling along the paraspinal (multifidus) muscles of the lumbar spine and over the sacrum is more convenient in the veterinary species and appears effective in this condition.

Having said that, many studies have explored the effects on the gut of stimulation of ST36 and postulate effects on an increase in vagal activity. Two experimental studies in dogs show some positive effects on intestinal transit and suggest that acupuncture may have an indication in functional problems of the canine gut. The Sun study ( $n=6$ ) used bilateral EA to ST36 at 25 Hz and 6 mA (Sun et al., 2010). Yin et al. (2010) looked at the effect of EA on rectal distension-induced delay in solid gastric emptying (a proposed model for irritable bowel syndrome dominated by constipation in human patients) and also used bilateral stimulation of ST36 with 25 Hz at 6 mA, comparing this with 'sham EA' – needles placed 'off meridian' in the thighs about 20 cm from ST36 with no electrical stimulation; with control; and with EA plus naloxone. EA accelerated the gastric emptying compared with control; sham EA had no effect; and the naloxone blocked the effects of EA.

'Grass sickness', or equine dysautonomia, is a distressing condition of horses that can present acutely with failure of gut function and is often fatal, but there are more chronic presentations where some gut function remains, and there have been some reports of acupuncture helping the management of this condition. Again a segmental approach would be indicated, targeting the dorsal paraspinal muscles.

Ileus commonly occurs postoperatively in horses, and in rabbits when they stop eating, after surgery, interventions or illness. Whilst no studies have been done and no case reports noted, these ought to be good candidates for the use of acupuncture.

### **Nausea and vomiting**

There is one study that suggests vasopressin-induced vomiting in dogs can be suppressed by acupuncture at PC6 but not at ST36 or BL21. The authors suggest that the effect is mediated by a central opioid pathway, but it is not clear why the other points would not stimulate the same pathway (Tatewaki et al., 2005).

## **FERTILITY**

At the beginning of this chapter it was noted that acupuncture was probably used in domestic animals when they became of tangible value to their owners who needed to preserve their function for as long as possible. One major function is to reproduce, to increase the numbers of the species owned, but also to trigger lactation in the cow, sheep and goat. It should not be surprising therefore that there are a number of papers and reviews speculating on the use of acupuncture to enhance fertility in the sow, cow and horse (Schofield, 2008). Observed positive effects on fertility in these species may be achieved by optimising blood flow in the uterine artery as is reported in humans (Stener-Victorin et al., 2000), but there may also be a secondary effect of treating concurrent pain and thereby reducing stress and making conception more likely.

### **Summary of indications**

Acupuncture appears to have been used for most conditions presented in domestic animals, including farm animals and exotic species not described here. This is not surprising since historically many veterinarians could only learn acupuncture by learning traditional approaches. The traditional approach will always result in a diagnosis, and there will always be a treatment. A clinician using the western approach looks at the orthodox diagnosis and tries to work out from neurophysiological principles whether acupuncture is likely to work for the problem, which signs (symptoms) are likely to be improved by acupuncture (e.g. pain and or function; nausea; immunomodulation; anxiety) and, based on the examination of the animal, where to place the needles. This approach is therefore more circumspect about the conditions that are likely to respond.

## **Advantages and disadvantages of veterinary acupuncture**

### **Pain relief**

Acupuncture can in some cases provide potent pain relief. Although it has not been demonstrated, this author suggests that prey species (the horse, the rabbit, the cow, the sheep) and the cat (because it is solitary and highly reactive) would be better responders to acupuncture than would the dog or man because these animals generally respond more profoundly to any physiological stimulus.

### **Tolerance of acupuncture**

Most animal patients seem to accept the treatment well. The range of reactions to needle insertion is similar to that of humans, i.e. some react dramatically and do not seem to like the sensation, whilst others barely seem to feel anything. Cats and rabbits accept the treatment remarkably well compared with the expectation of their owners. Many animals appear to become quite sedated either at the time or after treatment, but this is a subjective observation which should be compared with simply being 'nice' to a patient for a prolonged period of time.

### **Non-specific benefits of acupuncture treatment**

Veterinary surgeons have to spend more time handling their patients for diagnosis and delivery of treatment than many of their colleagues in the medical profession, yet still there is something satisfying about the ability to relieve pain by the direct action of a physical therapy such as acupuncture. Although the therapy can be delivered relatively quickly, it is almost inevitable that once the needles are in place a greater time than usual is spent interacting with the client and animal. This time can be usefully spent educating the client further about the animal's condition and the importance of various treatments (pain control especially), but a secondary effect of this is the bonding that occurs between patient, client and clinician, leading to greater professional and personal satisfaction. What other effect this may have on the patient can at this time only be imagined, but they may well be significant.

### **Perception of safety**

There is an assumption that all things perceived as natural must be safe, but there are potential safety issues with acupuncture in animals, although currently very few reported problems in practice (this may simply be because there is no formal centralised collection of such data). The safety issues are similar to most of those in humans, the main cautions being for immunosuppressed patients; those with bleeding disorders; and the potential for causing septic arthritis and bleeding and bruising. Needle breakage is reported in three horses: one which reared and broke the needle against the roof beam of the stable, and two needle fragments left in after needle removal. For dogs the main danger in terms of the needles themselves would be consumption of the needle, especially in breeds that are unselective about what they eat, such as the labrador. Pneumothorax, the most common serious adverse side effect of acupuncture in humans, has not been reported in animals following needling. This may be because of shorter life spans so that the lungs have fewer pathological lesions, i.e. fewer bullae or blisters; it may have occurred but no connection has been made between the treatment and the condition; and because it is easier to avoid needling between the ribs because the veterinary species tend to have barrel-shaped chests to which it is easier to place the needles at a tangent.

### **Costs of treatment**

Apart from safety issues (and it must be remembered that, short of masterly inactivity, acupuncture will be one of the safest procedures most veterinarians will routinely perform), there are few real disadvantages to the use of acupuncture in veterinary practice. The costs may be prohibitively

high for some clients because the time of a clinician is often more expensive than the medication that they may prescribe. Most pet insurance companies will cover the cost of acupuncture, but pet insurance is still taken up by relatively few pet owners.

The cost of acupuncture treatment may also be measured in terms of time given up by the client, and the commitment of regular appointments may be too much for some.

### **Welfare of the patients**

Very few animals find the treatment so stressful that it becomes a significant barrier to using acupuncture on animals. In these cases where the patients are distressed the treatment simply would not be pursued unless it were felt that it was imperative to the animal's overall welfare, in which case sedation can be easily used to facilitate acupuncture.

## **Concluding comments**

Veterinary acupuncture is practised across the species: companion animals, farm species, birds and reptiles. Reports of success are widespread, but good quality evidence of effect is limited. However, whilst the technique is relatively safe and the perceived benefits appear significant, the pragmatists should continue to practise and hope that those in a position to do so are sufficiently inspired and enabled to produce convincing evidence that the alleviation of suffering in animals can be sometimes achieved by simple needling, as well as by complex chemicals.

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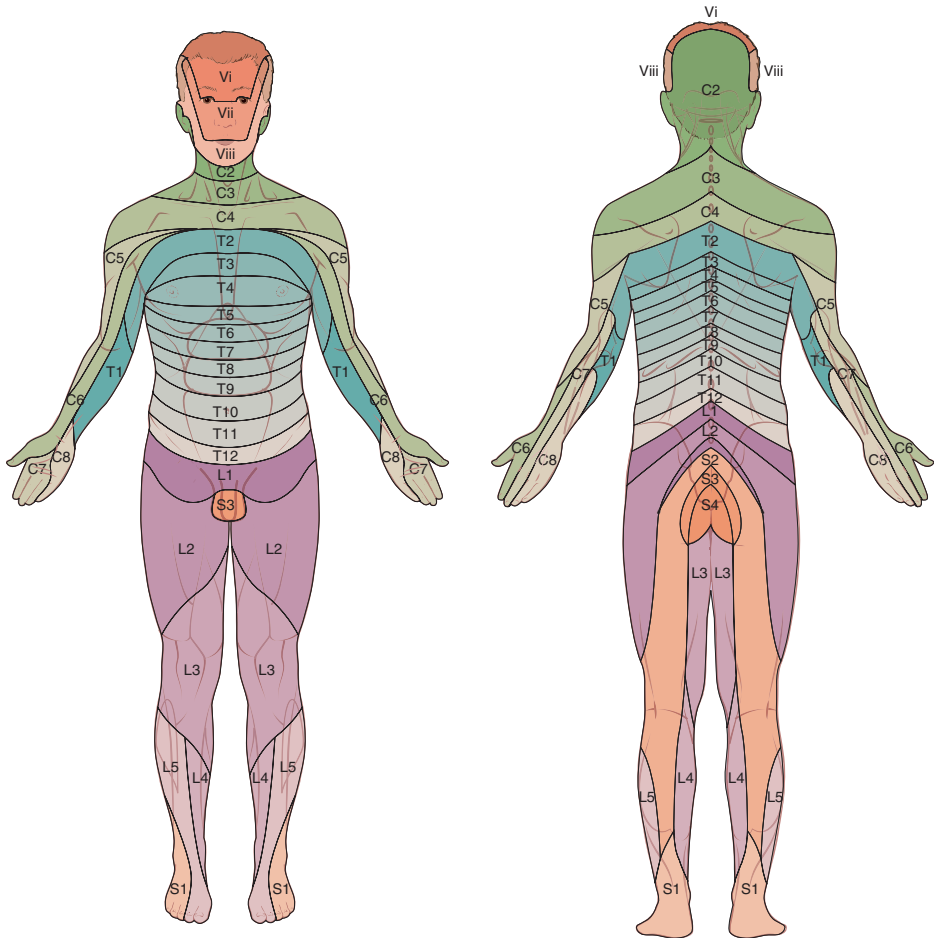
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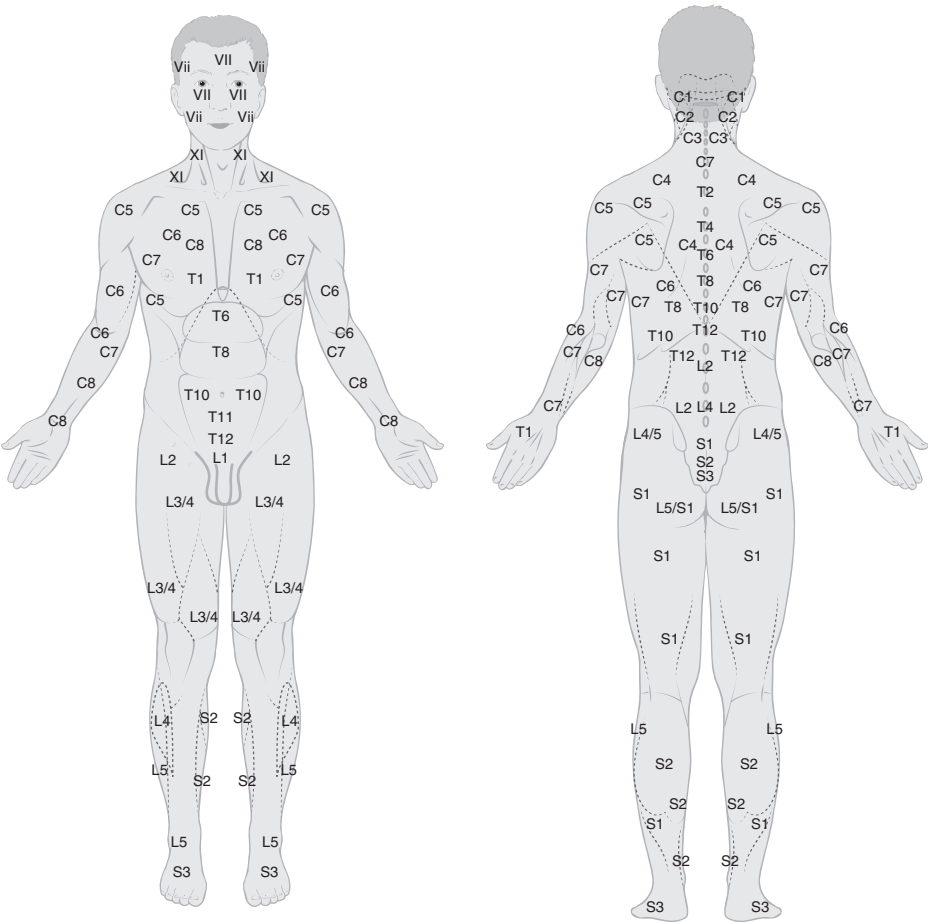
Appendix

SECTION OUTLINE	
1	Dermatome/myotome maps 665
2	Meridian/channel charts 667
3	Standard international nomenclature for the 14 meridians 687

# Dermatome/myotome maps



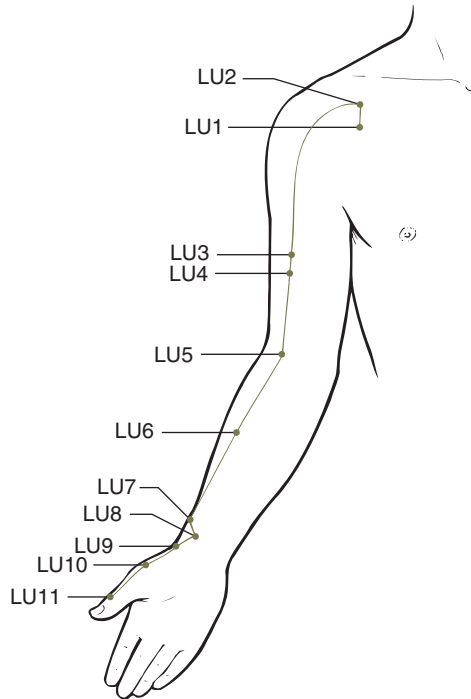
Dermatome map based on information derived from *Gray's Anatomy*.



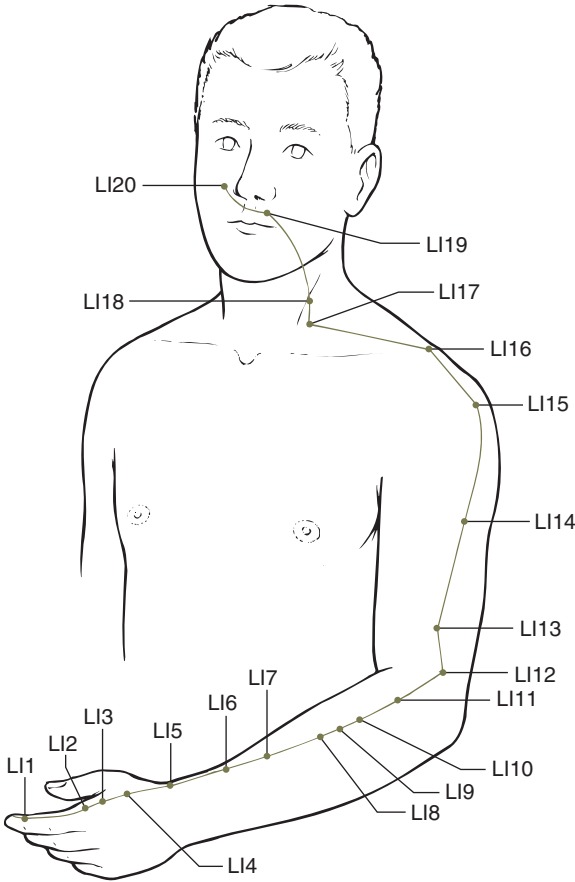
Myotome map for acupuncturists – this diagram illustrates the likely myotome target from needling into muscle tissue in the areas indicated by the segmental nomenclature. Derived from information included in *Gray's Anatomy*.

## Meridian/channel charts

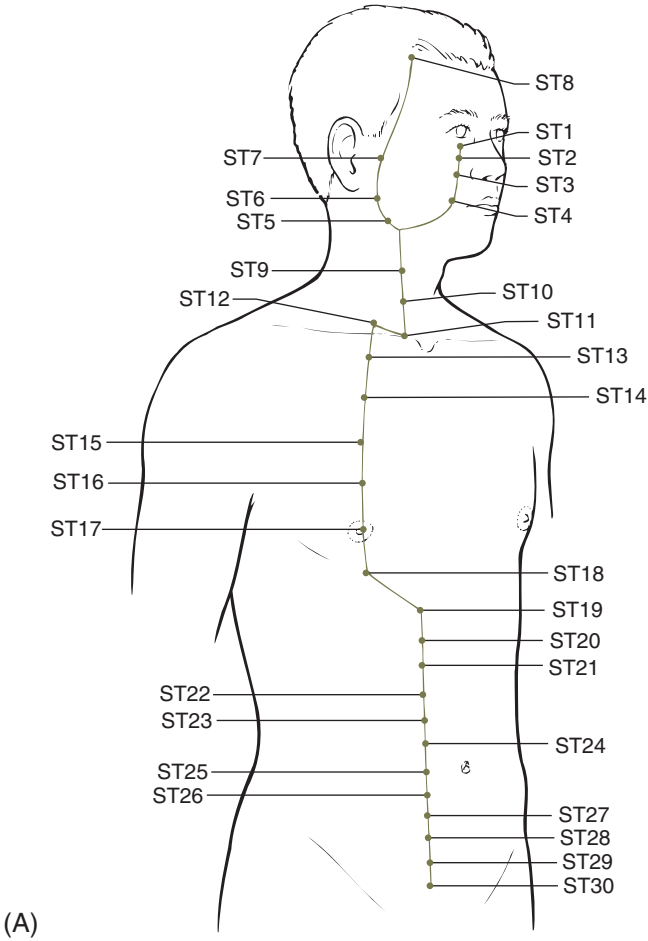
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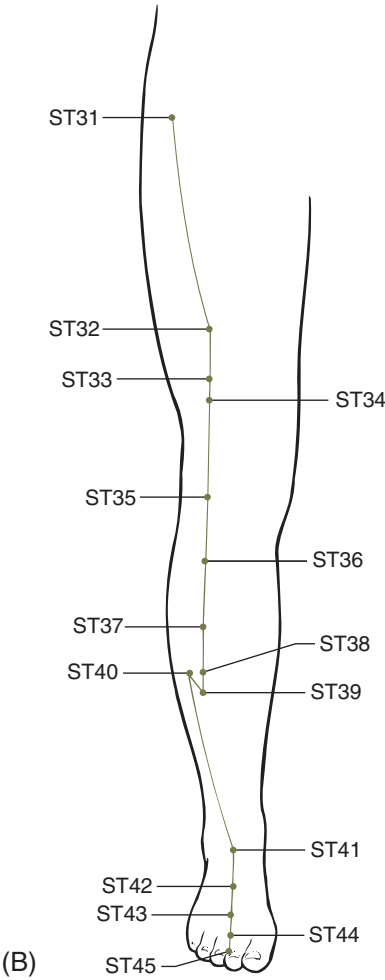
**App. 2.1** The Lung channel.



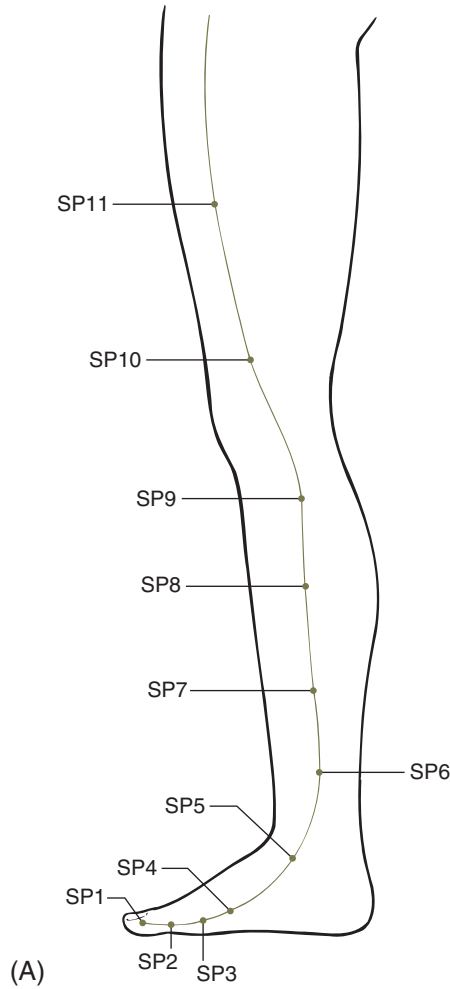
**App. 2.2** The Large Intestine channel.



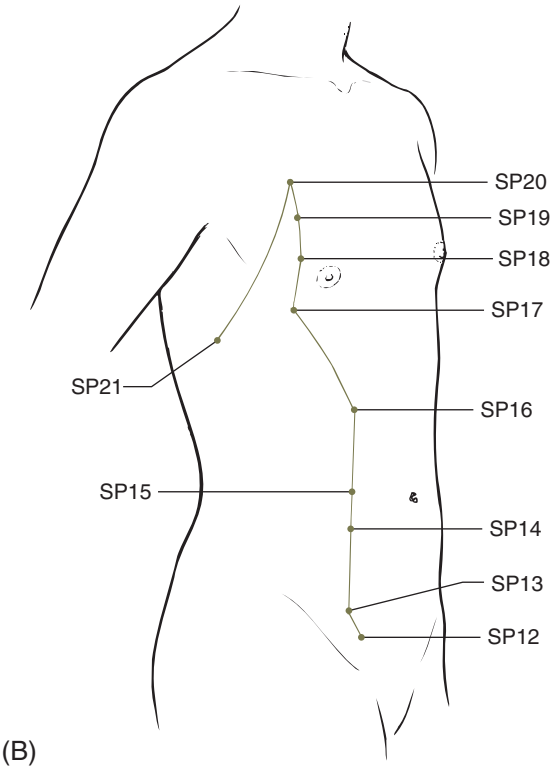
**App. 2.3A** The Stomach channel.



**App. 2.3B** The Stomach channel.

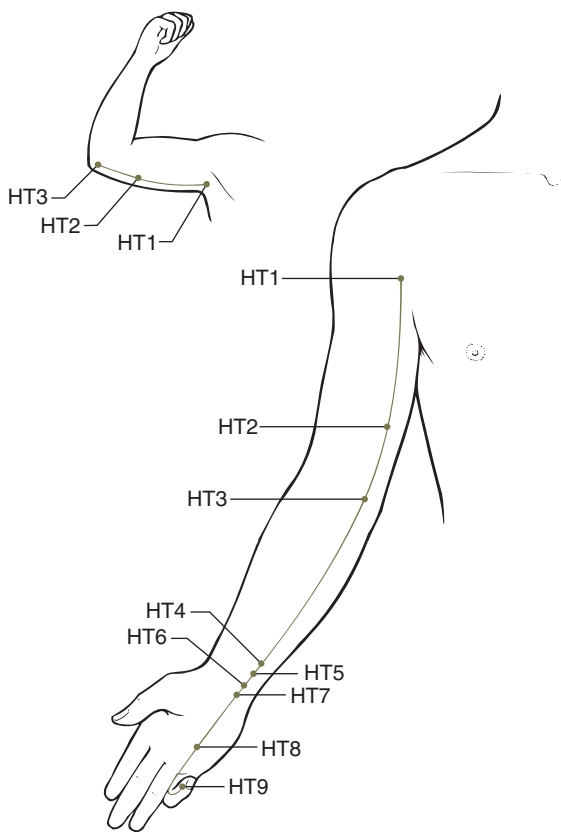


**App. 2.4A** The spleen channel.

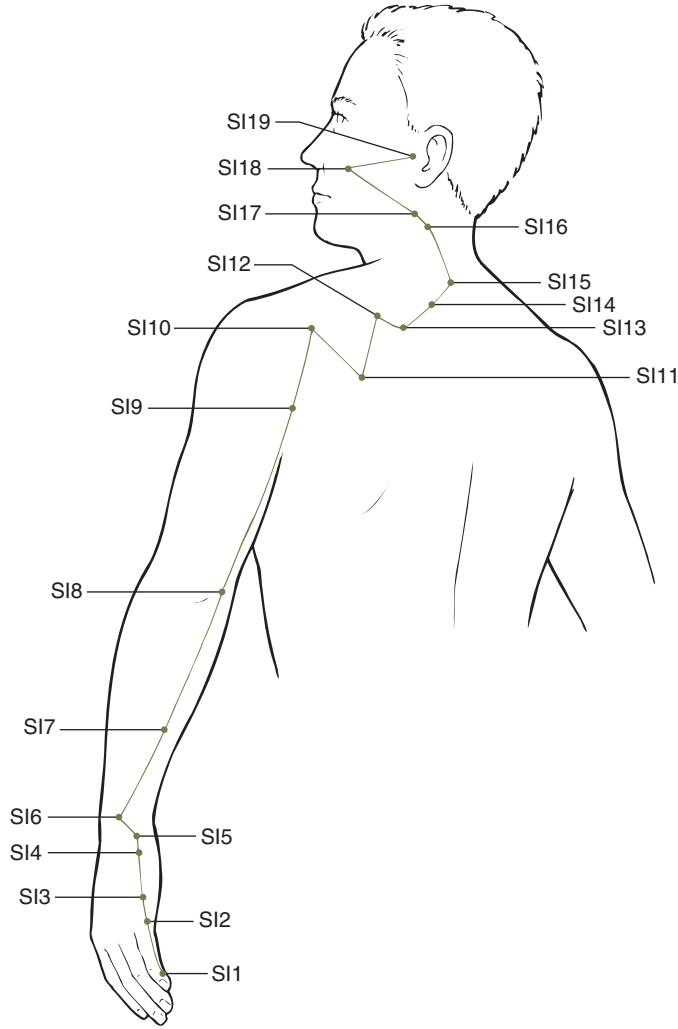


(B)

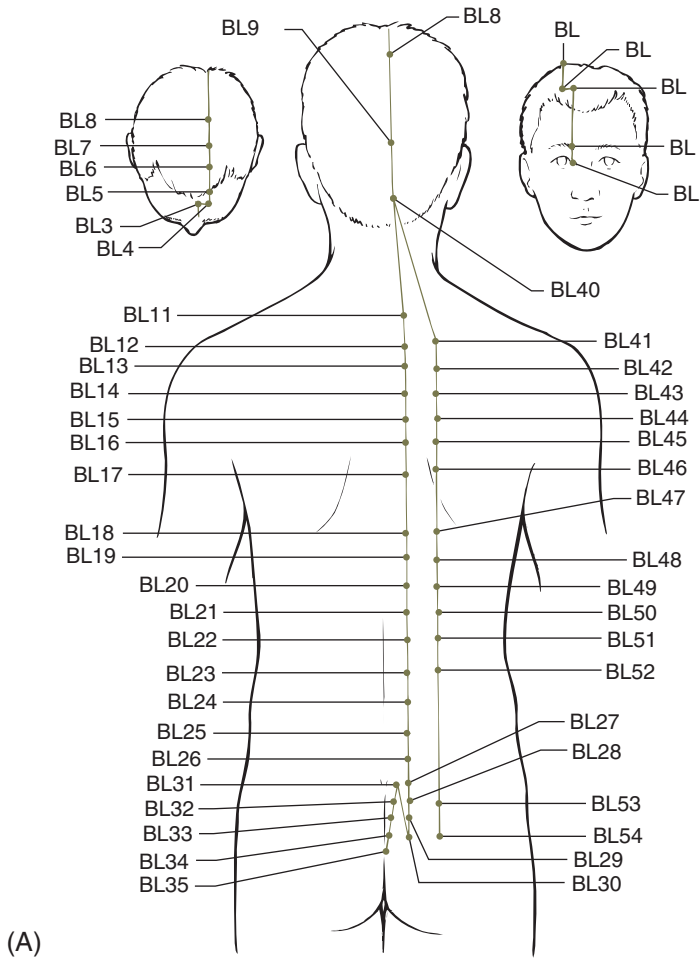
**App. 2.4B** The spleen channel.



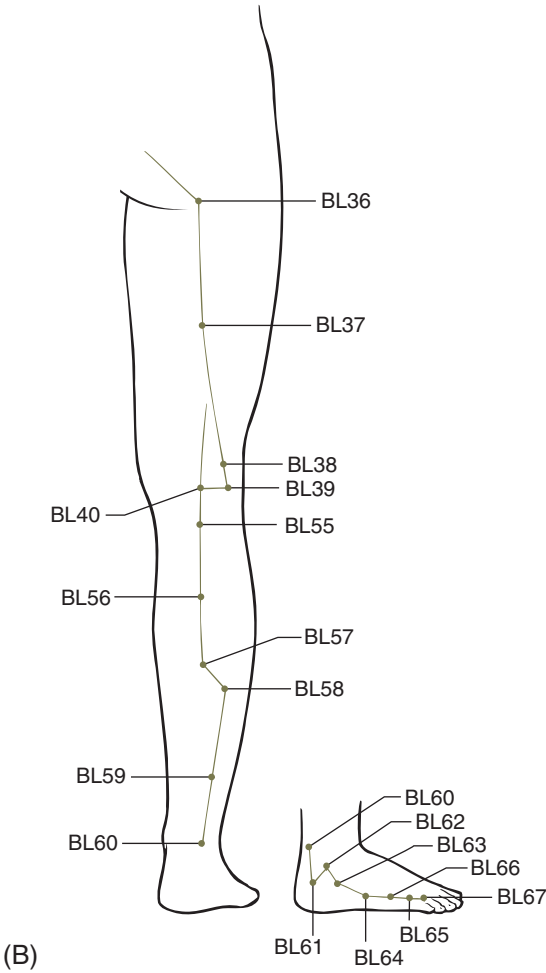
**App. 2.5** The Heart channel.



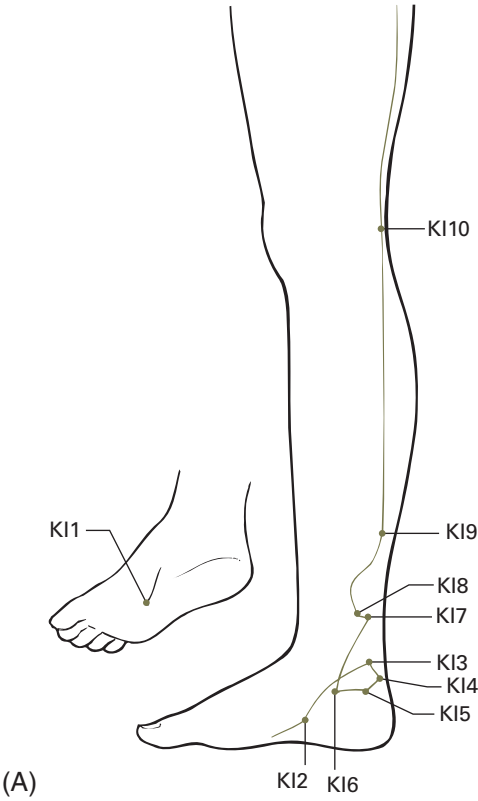
**App. 2.6** The small intestine channel.



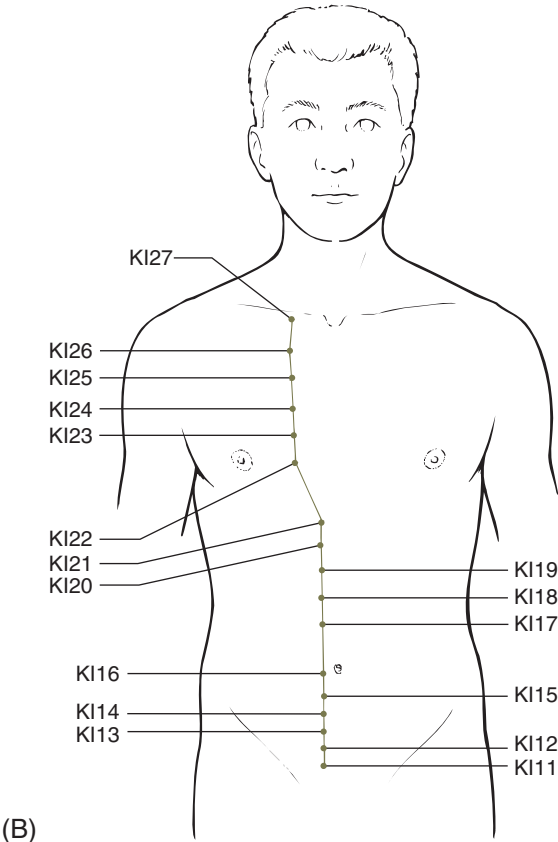
**App. 2.7A** The Bladder channel.



**App. 2.7B** The Bladder channel.

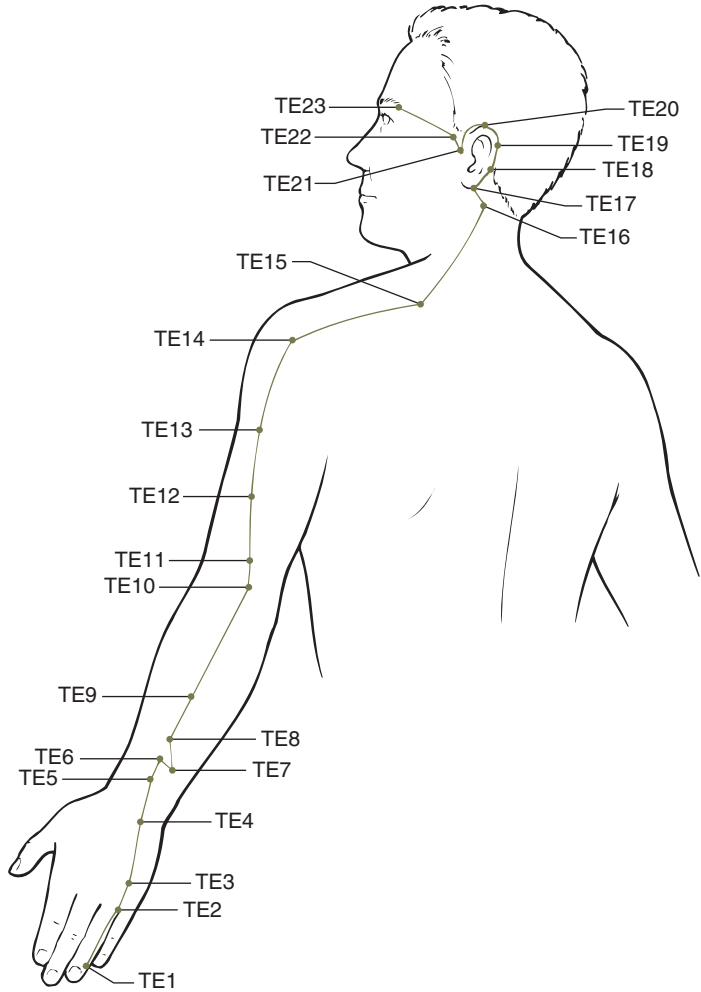


**App. 2.8A** The kidney channel.

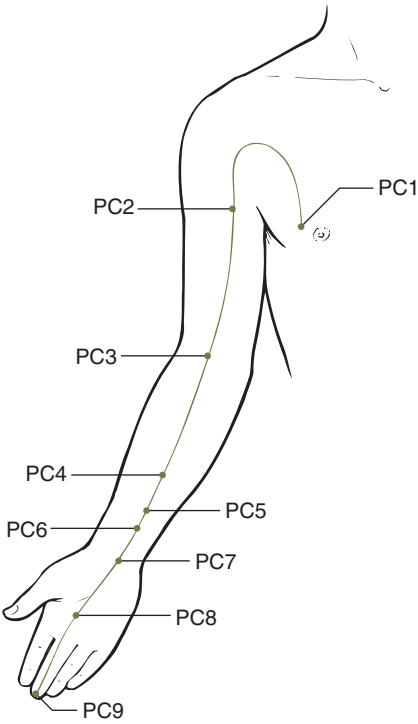


(B)

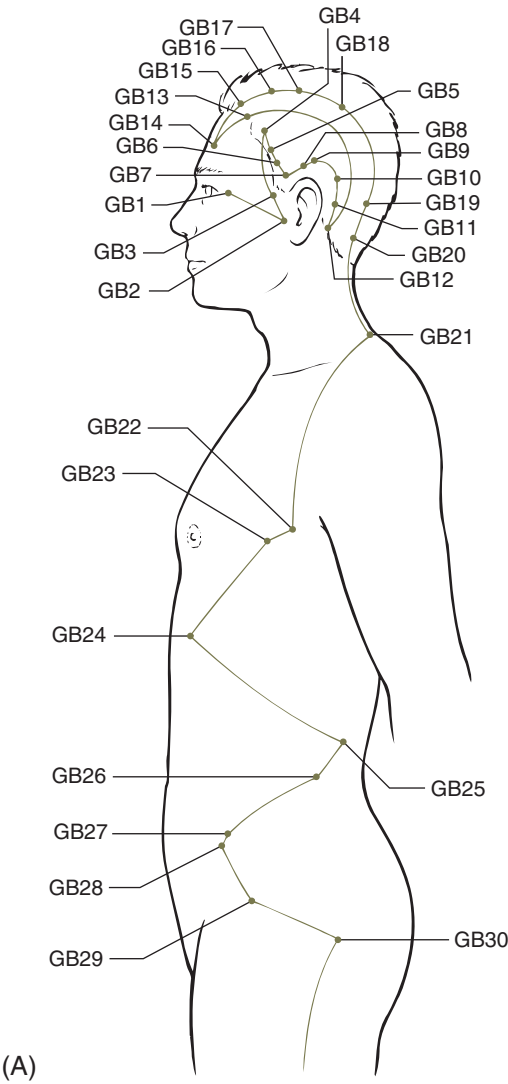
**App. 2.8B** The kidney channel.



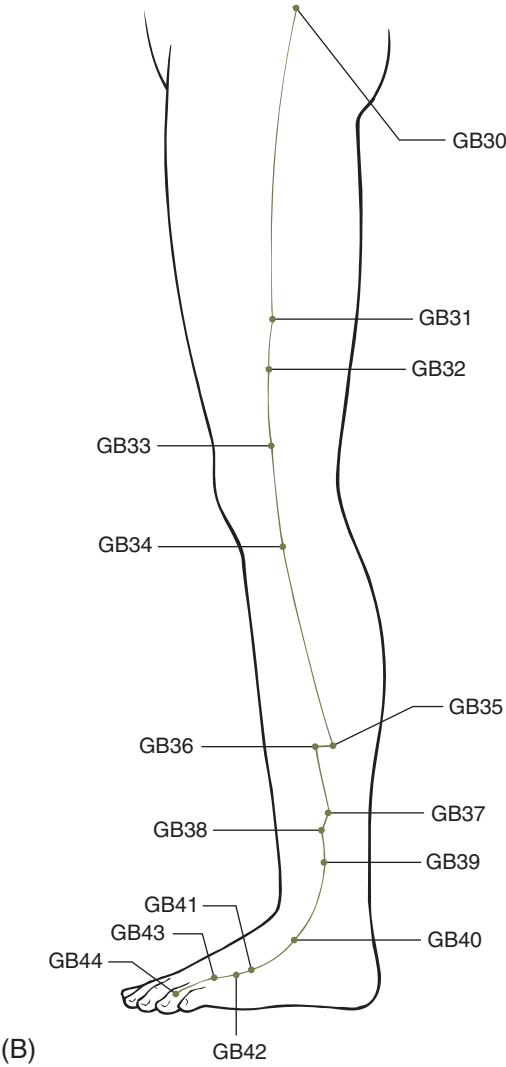
**App. 2.9** The triple energiser channel.



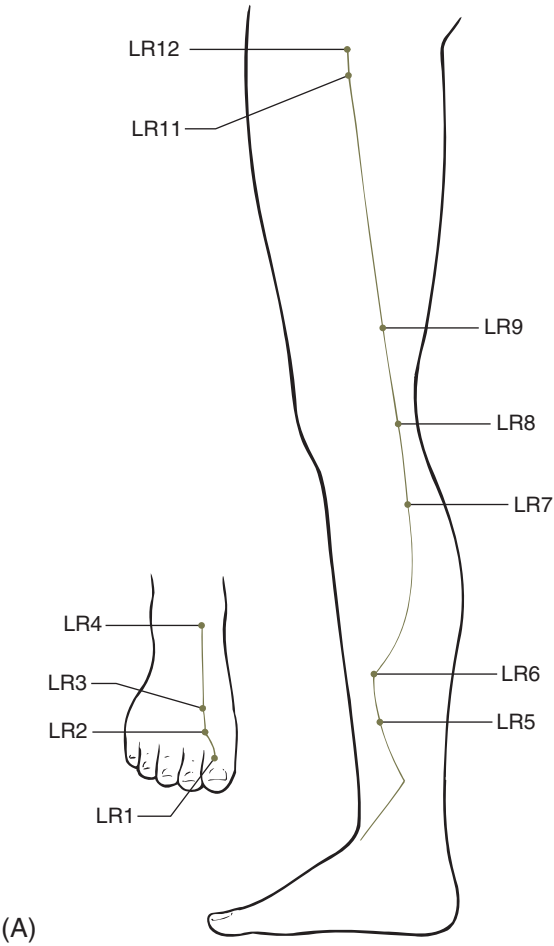
**App. 2.10** The pericardium channel.



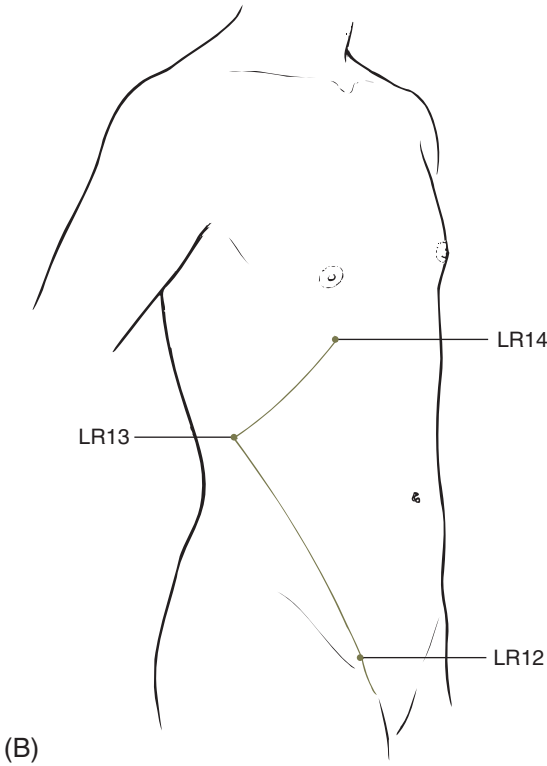
**App. 2.11A** The gall bladder channel.



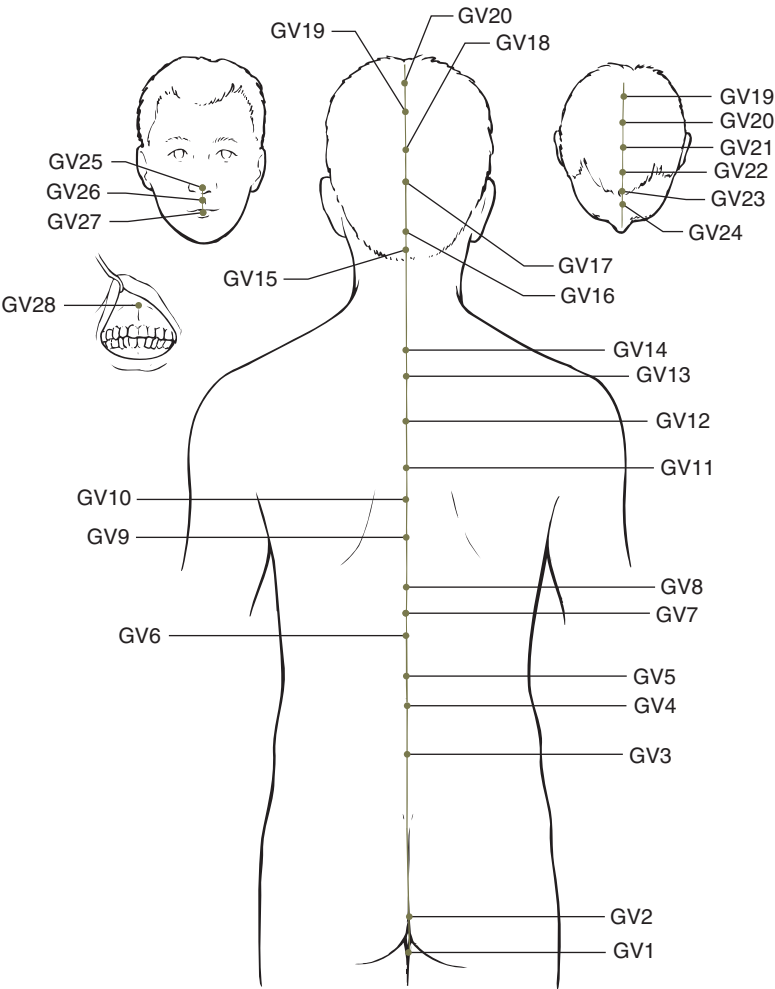
**App. 2.11B** The gall bladder channel.



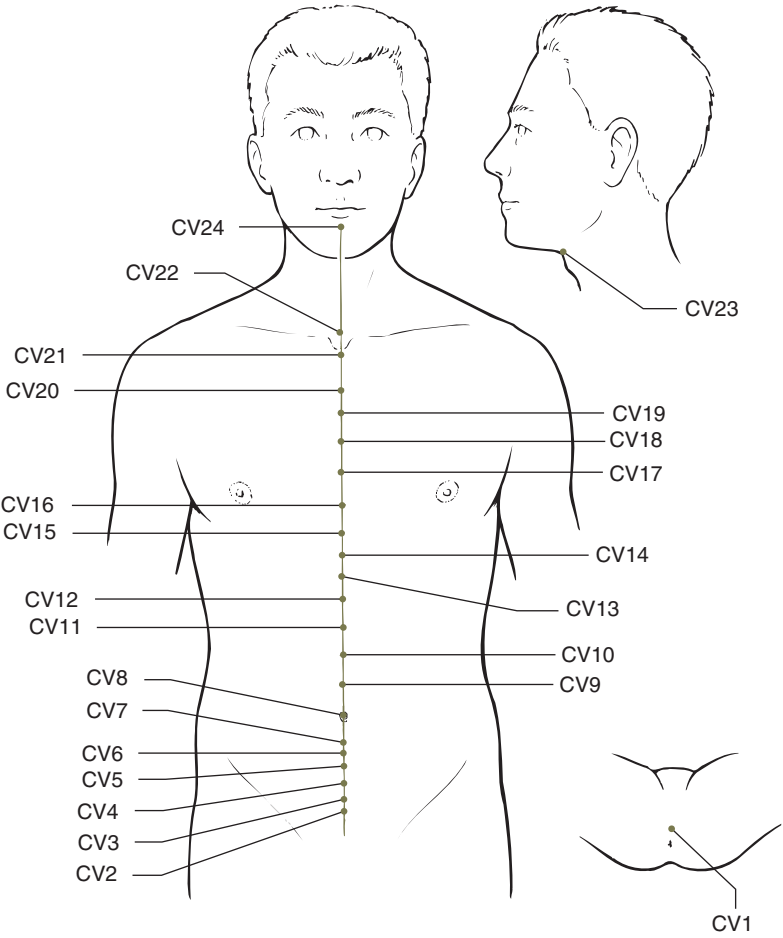
**App. 2.12A** The liver channel.



**App. 2.12B** The liver channel.



**App. 2.13** The Governor channel.



**App. 2.14** The Conception channel.

# Standard international nomenclature for the 14 meridians

Name of meridian	Alphabetic code	
	Agreed	Former
Lung	LU	Lu, P
Large intestine	LI	CO, Co, IC
Stomach	ST	S, St, E, M
Spleen	SP	Sp, LP
Heart	HT	H, C, Ht, He
Small intestine	SI	Si, IT
Bladder	BL	B, Bi, UB
Kidney	KI	Ki, R, Rn
Pericardium	PC	P, Pe, HC
Triple energiser	TE	T, TW, SJ, 3H, TB
Gall bladder	GB	G, VB, VF
Liver	LR	Liv, LV, H
Governor vessel	GV	Du, Du Go, Gv, TM
Conception vessel	CV	Co, Cv, J, REN, Ren

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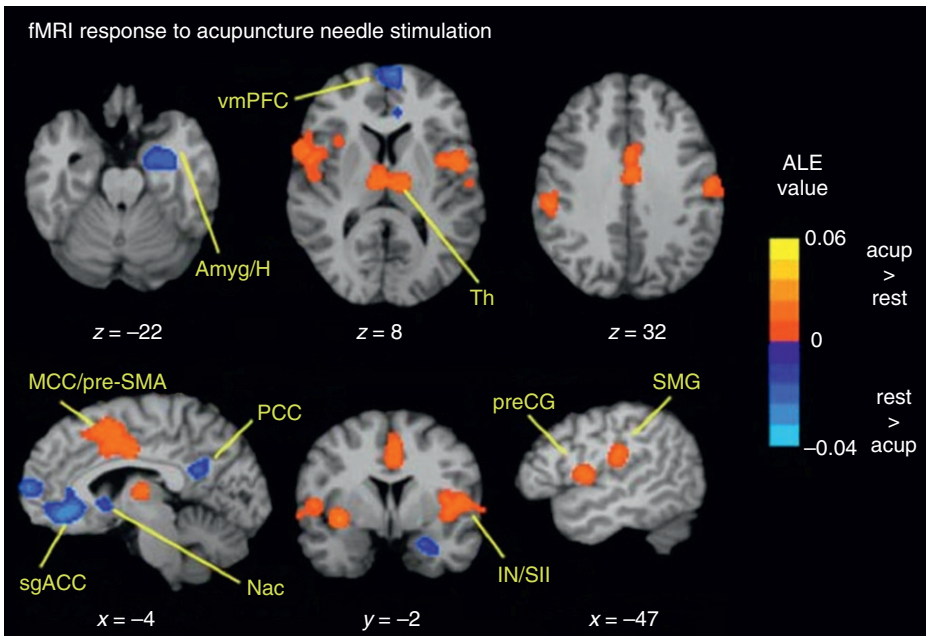
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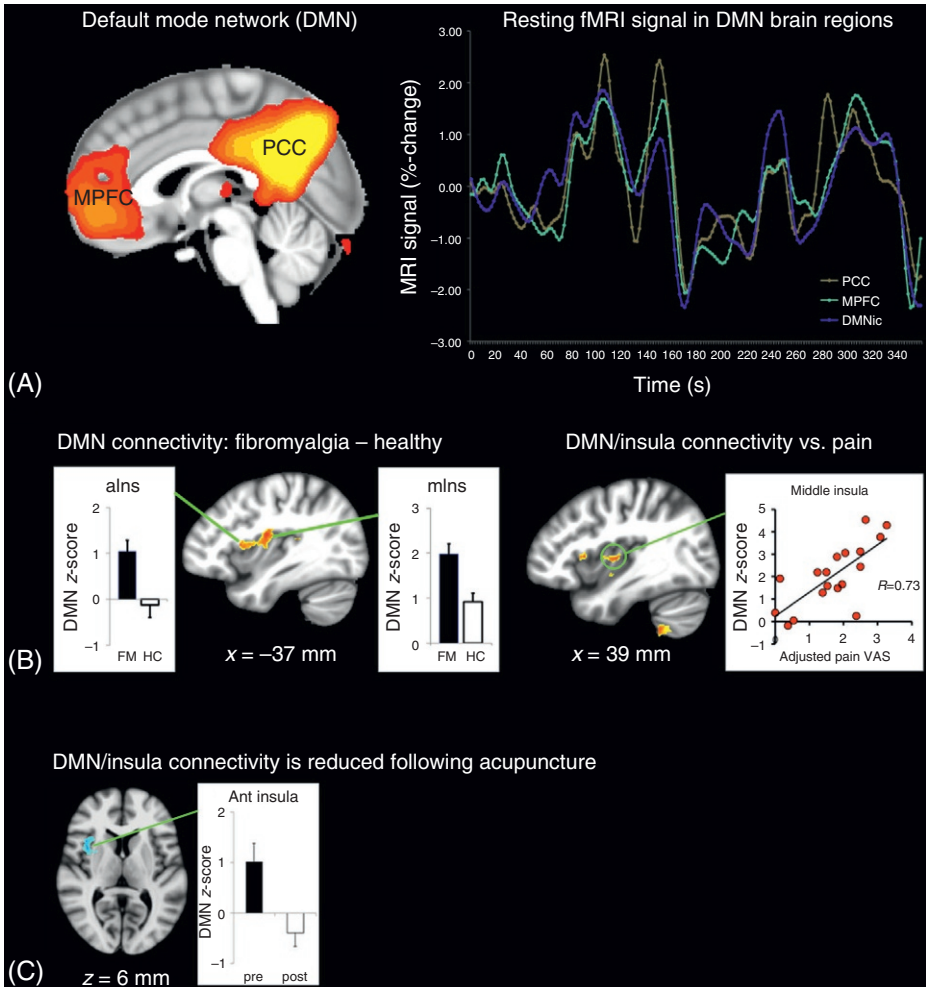
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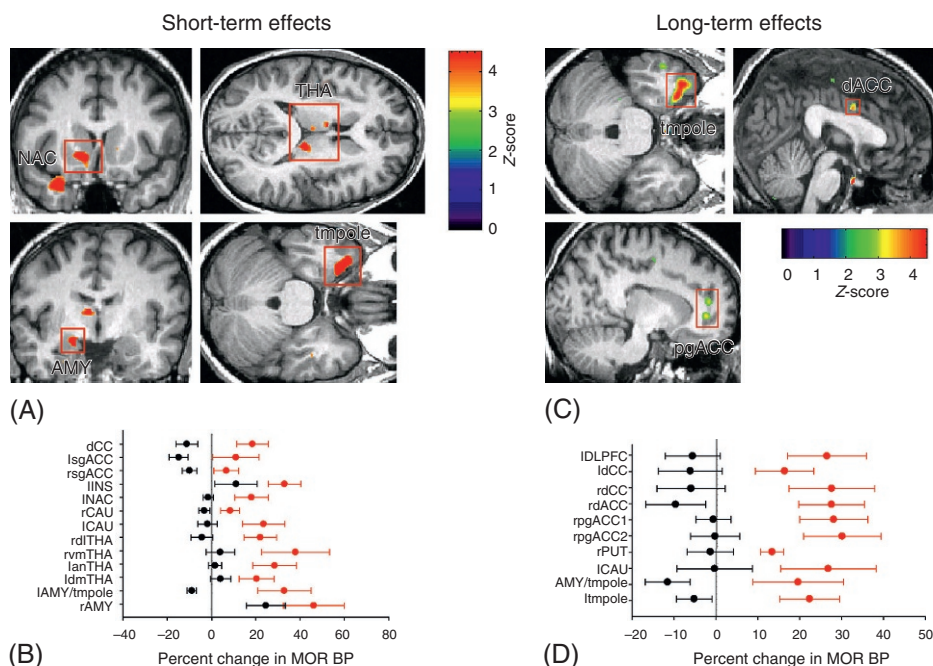
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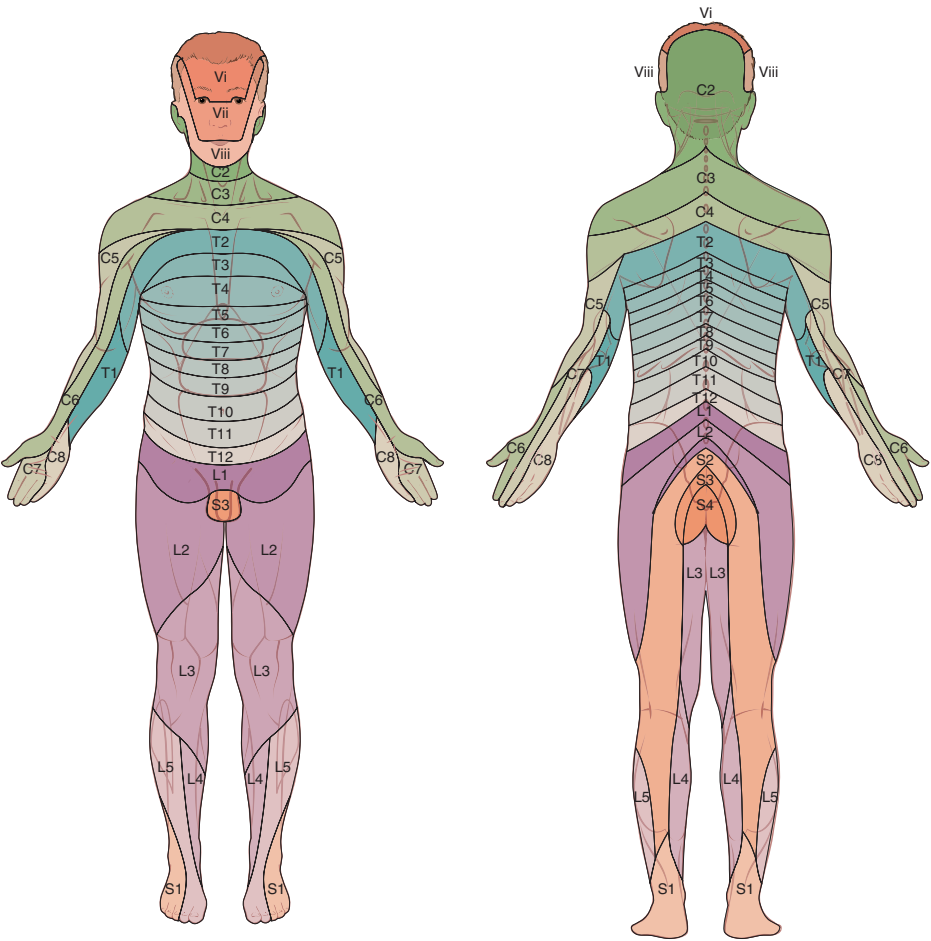
**Figure 4.1** A meta-analysis of 34 fMRI studies characterising brain responses to acupuncture found a common response pattern across studies where somatosensory (S1, S2, thalamus) and stimulus salience (insula, mid-cingulate) regions were activated, while affective limbic (amygdala, Nac, DMN) regions were deactivated. Note: amygd, amygdala; DMN, default mode network; fMRI, functional magnetic resonance imaging; IN, insula; MCC, middle cingulate cortex; Nac, nucleus accumbens; PCC, posterior cingulate cortex; sgACC, subgenual anterior cingulate cortex; SII, secondary somatosensory cortex; SMA, supplementary motor area; SMG, supramarginal gyrus; Th, thalamus; vmPFC, ventromedial prefrontal cortex. (Reproduced from Huang, W., Pach, D., Napadow, V., Park, K., Long, K., Neumann, J., et al., 2012. Characterizing acupuncture stimuli using brain imaging with fMRI – a systematic review and meta-analysis of the literature. *PLoS One* 7 (4), e32960.)



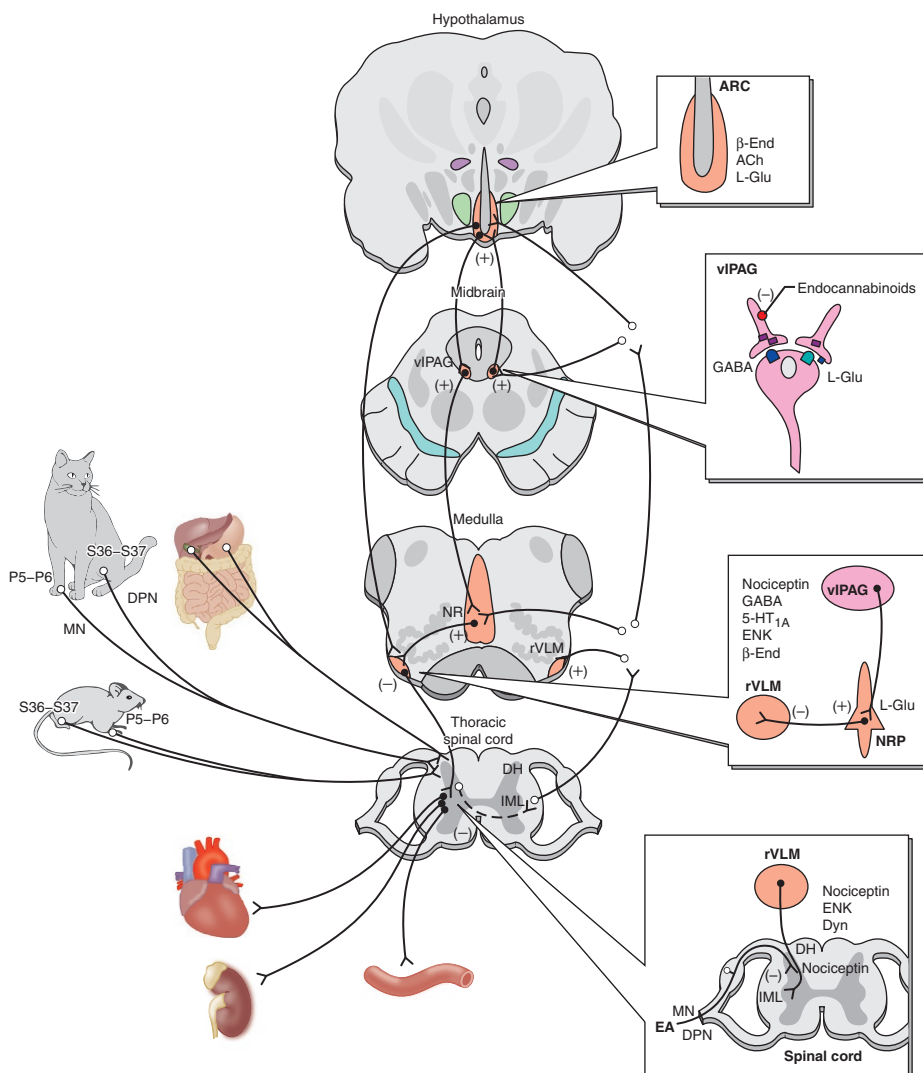
**Figure 4.2** Acupuncture modulates resting brain connectivity in chronic pain patients. **(A)** Functional magnetic resonance imaging (fMRI) can be used to assess resting functional connectivity within and between different brain regions and networks, such as the default mode network (DMN), where fMRI signal between the medial prefrontal cortex (MPFC) and posterior cingulate cortex (PCC) is highly correlated. **(B)** Chronic pain patients suffering from fibromyalgia (FM) have increased resting DMN connectivity to the insula, and this connectivity is greater with greater pain reported at the time of the scan (Napadow et al., 2010). **(C)** Acupuncture (both sham and verum) were found to reduce pain and reduce DMN/insula connectivity (Napadow et al., 2012a,b).



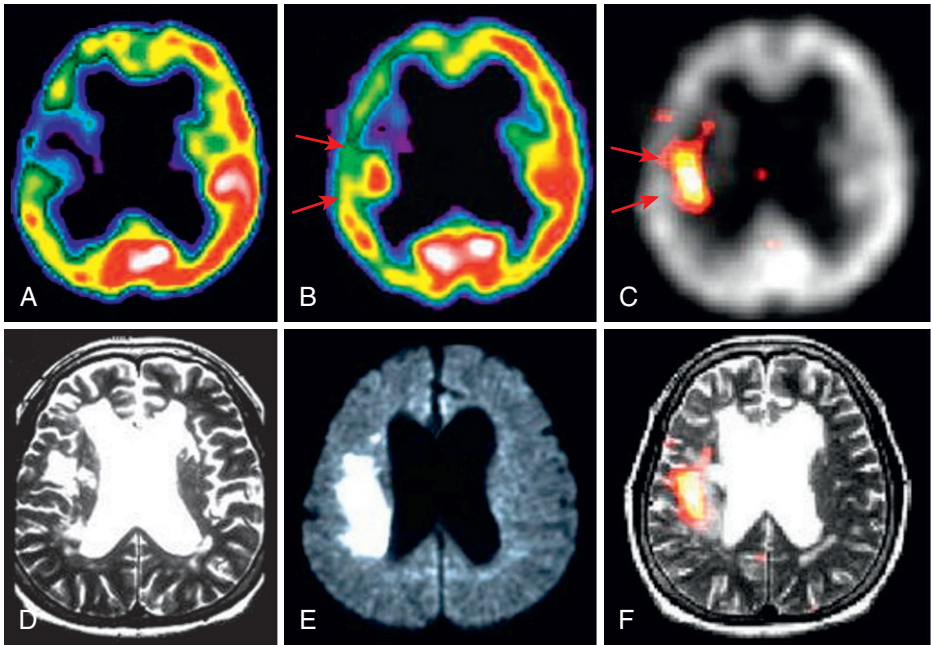
**Figure 4.3** Differential short-term and long-term effects of acupuncture and sham acupuncture on MOR binding potential (BP). **(A)** Regions of interest showing increased MOR BP following acupuncture as compared to sham treatment. *Upper left:* left nucleus accumbens (lNAC), *upper right:* three thalamic regions (THA), *lower left and right:* left amygdala (lAMY) and temporal pole (ltmpole), respectively. **(B)** Short-term percent changes in MOR BP for all regions identified. Red circles (TA) and black circles (SA) represent group mean values with standard error bars. Overall acupuncture resulted in increases in MOR BP with sham treatment resulting largely in either no change or small decreases in BP. **(C)** Regions of interest showing long-term increased MOR BP following acupuncture as compared to sham treatment. *Upper left:* temporal pole (ltmpole), *upper right:* dorsal anterior cingulate cortex (dACC), *lower left:* two perigenual anterior cingulate regions (pgACC). **(D)** Percent changes in MOR BP for all regions identified. Red circles (TA) and black circles (SA) represent group mean values with standard error bars. Overall acupuncture resulted in long-term increases in MOR BP whereas sham treatment resulted in either no change or a decrease in binding ability.



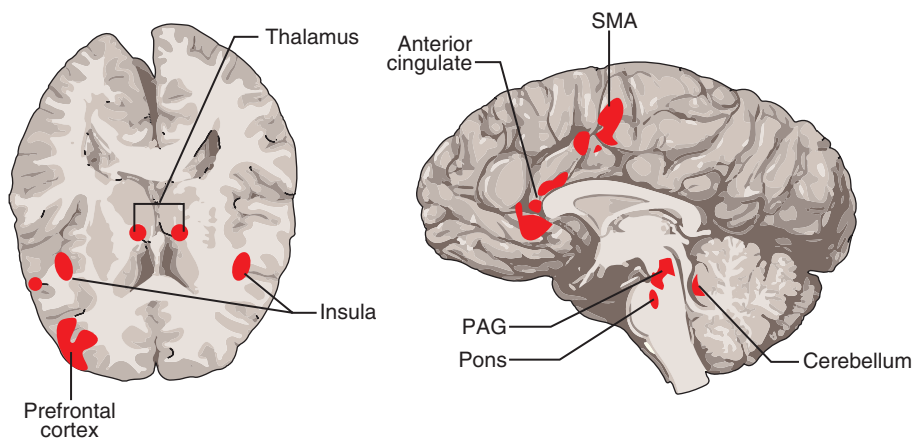
**Figure 7.1** Dermatome map based on information derived from Gray's Anatomy.



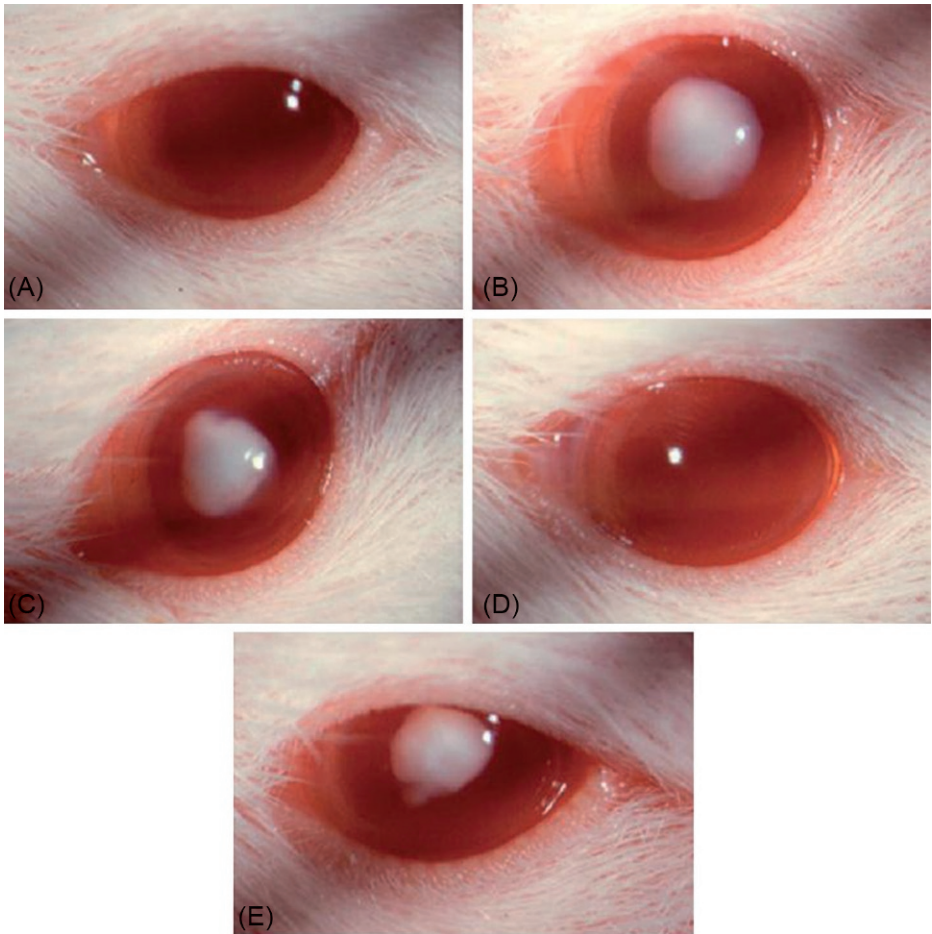
**Figure 23.3** Neural circuitry of acupuncture's action on visceral reflex-induced changes in cardiovascular sympathetic outflow following application of bradykinin (BK) to the gallbladder of cats or distension of the stomach in rats. Electroacupuncture at PC5 + PC6 and ST36 + ST37 somatic acupuncture points stimulates the median (MN) and deep peroneal nerves (DPN) evoking activity in the arcuate nucleus (ARC) in the ventral hypothalamus, ventrolateral periaqueductal grey (vPAG) in the midbrain, nucleus raphe (NR) especially the NR pallidus (NRP) and rostral ventrolateral regions of the medulla (rVLM) as well as the dorsal horn (DH) and intermediolateral column (IML) of the spinal cord. A number of neurotransmitters, including acetylcholine (ACh), L-glutamate (L-Glu),  $\beta$ -endorphin ( $\beta$ -End), endocannabinoids,  $\lambda$ -aminobutyric acid (GABA), met- and leu-enkephalin (Enk), serotonin or 5-hydroxytryptamine (5-HT), nociceptin and dynorphin (Dyn) in the brain and spinal cord have been shown to participate in these brain nuclei by either activating (+) or inhibiting (–) neural activity evoked by the primary visceral reflex during EA modulation. The long pathway between the ARC and the rVLM illustrates the primary source of  $\beta$ -End. See text for details. (Reproduced from Li, P., Longhurst, J.C., 2010. *Neural mechanism of electroacupuncture's hypotensive effects*. *Auton. Neurosci.* 157, 24–30, with permission of Elsevier.)



**Figure 24.1 (A–F)** Increased regional cerebral blood flow (rCBF) in the ischaemic zone after acupuncture. **(A)** Baseline perfusion single-photon emission computed tomography (SPECT) obtained 3 weeks after symptom onset in a patient with right middle cerebral artery (MCA) occlusion shows perfusion defect in right frontal lobe with surrounding hypoperfusion. **(B)** SPECT 8 days later shows acupuncture-induced increased rCBF in the hypoperfused zone (*arrows*). **(C)** Subtraction of the baseline and postacupuncture image shows this more clearly (*arrows*). **(D, E)** T2- and diffusion weighted MRI (DWI): the area giving normal signal in **D** high signal intensity in **E** is taken to represent cytotoxic oedema within the viable ischaemic zone. **(F)** Superimposition of **C** and **D**: acupuncture-induced increase in rCBF occurred in the peri-infarct ischaemic zone. (*Reproduced from Lee, J.D. et al., 2003. The cerebrovascular response to traditional acupuncture after stroke. Neuroradiology 45, 780–784. Figure 1, © Springer-Verlag 2003, with kind permission from Springer Science + Business Media.*)



**Figure 27.1** Brain areas involved in the regulation of urine storage. The thalamus, insula, prefrontal cortex, anterior cingulate, periaqueductal grey (PAG), pons, medulla and supplementary motor area (SMA) are involved in the regulation of urine storage. (Reproduced from Fowler, C.J., Griffiths, D., de Groat, W.C., 2008. *The neural control of micturition*. *Nat. Rev. Neurosci.* 9 (6), 453–466 with permission of the publisher.)



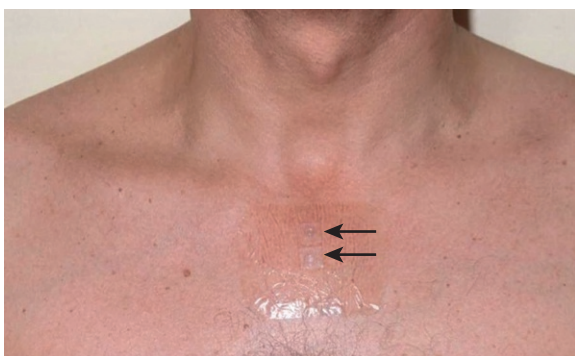
**Figure 30.1** Acupuncture for cataract prevention. Animal model of cataract induction by subcutaneous selenite injection. **(A)** Control group: no cataract. **(B)** Selenite injection: 100% cataract grade 4–6. **(C)** Selenite and anaesthesia: 100% cataract grade 4–5. **(D)** Selenite and EA under anaesthesia: 45% no cataract, 20% cataract grade 1–3, 35% grade 4–5. **(E)** Selenite and sham acupuncture under anaesthesia: 100% cataract grade 4–5 (Cariello et al., 2006).



**Figure 34.1** Treatment showing segmental and trigger points.



**Figure 34.2** Surround the dragon circling technique of needling.



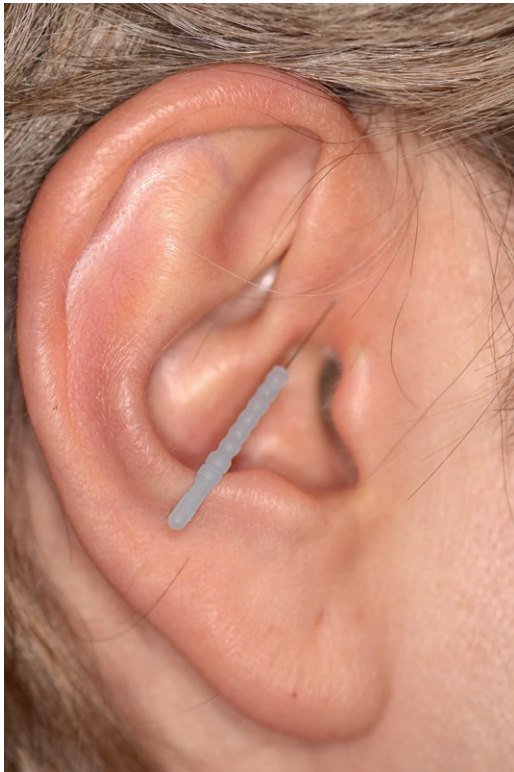
**Figure 34.3** Two points in the upper sternum known as ASAD points are commonly used in the UK for treating anxiety, sickness and dyspnoea.



**Figure 34.5** Indwelling needles at SP6 and self-administered 'one off' needling sites at SP6 and LR3.



**Figure 38.1** Point Conception Vessel 24 needled for control of gagging prior to dental treatment.



**Figure 38.2** Ear point 'Fiske' for control of gagging.